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A-90-16

A-90-16
IV-D-214

TOYOTA TECHNICAL CENTER, U.S.A., INC.
ANN ARBOR BRANCH
1588 WOODRIDGE, RR #7, ANN ARBOR, MI 48105, PHONE (313) 769-1350

March 1, 1991

Air Docket Section (LE-131)
U.S. Environmental Protection Agency
Room M-1500
401 M Street, S.W.
Washington, D.C. 20460

Attention : Docket No. A-90-16

Subject : Submission of Toyota's Emission Test Results with MMT Fuel Additive

Toyota submitted the interim emission test results dated October 26th 1990 for a vehicle durability program which had 1/32 g/gallon Mn MMT added to the test fuel.

We have just completed all tests, including additional reference tests for fuel without MMT. Although this data was obtained from one vehicle, the information is being supplied for your information.

The data shows that HC, CO and Particulate Emissions are all adversely affected by the MMT additive. The NOx Emissions were not dramatically affected. The increase in HC corresponds to our past test results with 1/16 g/gallon Mn MMT attached to our comments dated July 20, 1990.

If there are any questions regarding the enclosed information, please contact Mr. K. Kibe of my staff.

Sincerely,

Takao Niwa

Takao Niwa
General Manager
Emission Certification

cc : Ms. Mary T. Smith

1. Test Vehicle and Engine

Vehicle : '90 MY Camry Sedan, 4 A/T
Engine : 3S-FE (2.0L, L4)
Emission Control System : Multipoint Electronic Fuel Injection + 2 Three Way Catalysts (Close-coupled and Underfloor catalysts) + 2 Oxygen Sensors

2. Test Conditions

(1) MMT Additive 1/32 g/gallon Mn

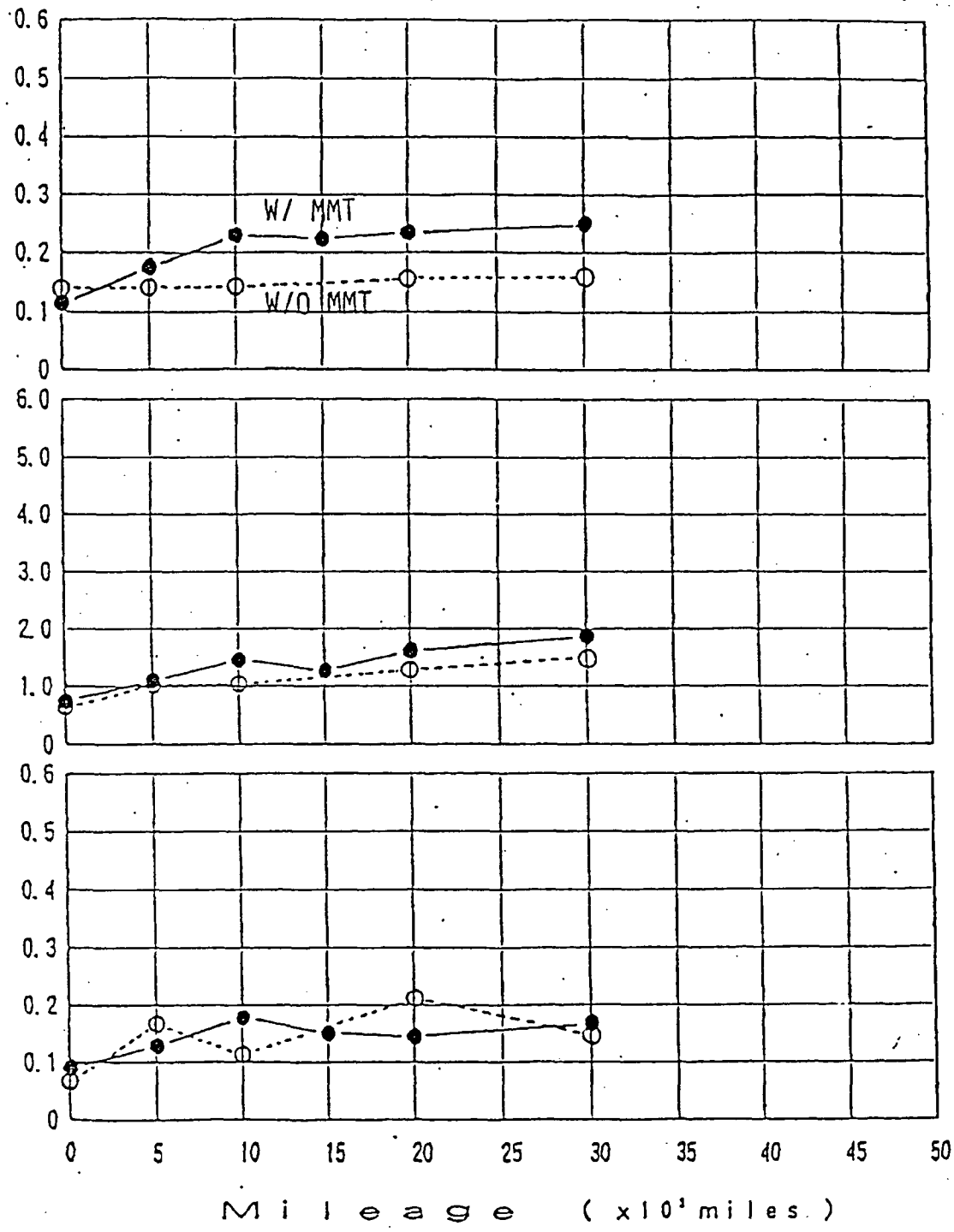
(2) Mileage Accumulation Fuel Characteristics

RON	91.4
MON	81.5
RVP	9.9 psi
Distillation Range	
IBP (Degrees F)	85
10%	119
50%	211
90%	343
EP	402
Olefins (vol. %)	6.8
Aromatics (vol. %)	36.5

(3) Mileage Accumulation Mode
Toyota in-house durability driving mode

(4) Emission Test Fuel
EPA certification test fuel

3. Test Results



Part.
(g/mile)
at 30 × 10³ miles

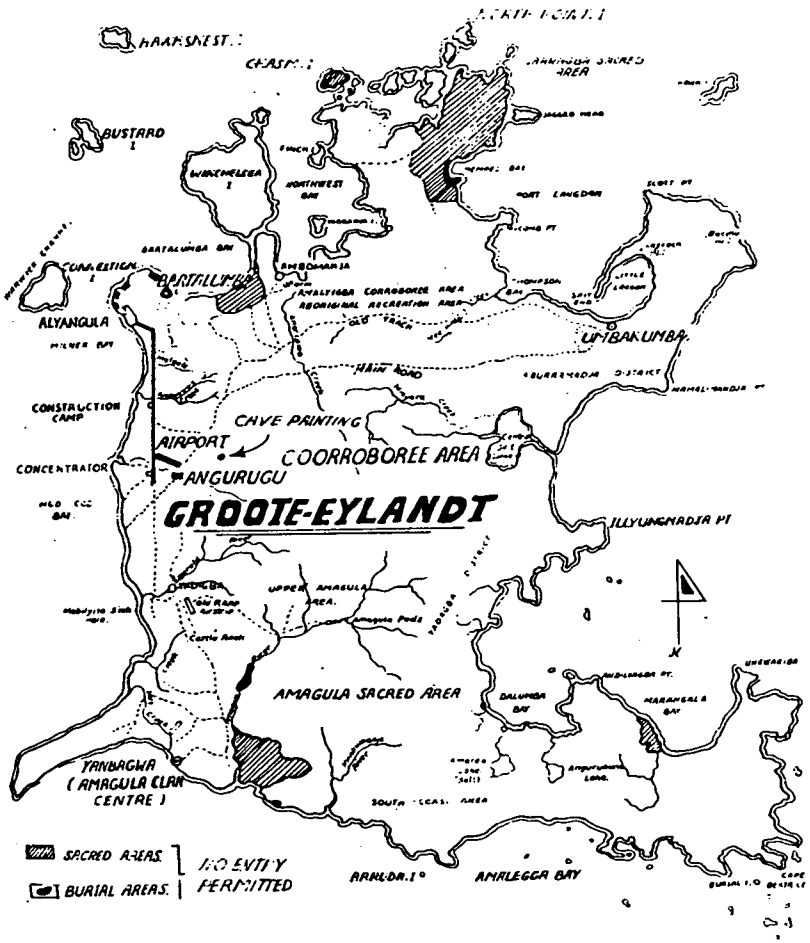
W/ MMT	0.0045
W/O MMT	0.0029

A-90-16

RESEARCH ON -

MANGANESE AND METABOLISM -

GROOTE EYLANDT, NORTHERN TERRITORY



Proceedings of a conference
held at Health House, Darwin, N.T.
on 11 June, 1987
at the invitation of
Dr Keith Fleming, Secretary for Health,
Northern Territory Department of Health

This report is for limited circulation, for the use of those who attended the Conference, or those who have a professional interest in the subject. It is not for sale.

Production: Mary Hammill

Illustrator: Billy Reid

Printing: University of Queensland Printery, St Lucia.

September 1987

FOREWORD:

Research is being conducted, at the request of the Angurugu Community, Groote Eylandt, into the unusual disease conditions prevalent there.

This publication reports the proceedings of the conference held in Health House of the N.T. Department of Health, Darwin, on 11 June, 1987.

Thanks for support in this venture are due to the following organizations:

The Northern Territory Department of Health
The Angurugu Community Council
The Groote Eylandt Mining Company Ltd
The Church Missionary Society
The National Health and Medical Research Council
The Menzies School of Health Research, Darwin
The Department of Aboriginal Affairs
The University of New South Wales

All contributed in their own way to this production.

Joint editors:-
Prof John Cawte and Dr Charles Kilburn
Schools of Psychiatry, and Paediatrics,
University of New South Wales

REASONS FOR CONVENING THIS CONFERENCE

Chairman: Professor John Cawte

The colloquium was held at the Health Department of the Northern Territory, Darwin, on 11th June, 1987. The agenda was to share new information about the neurological disorders and possibly other related conditions affecting people at Angurugu, Groote Eylandt, where there is an unusual mineral ambience.

The colloquium host was Dr Keith Fleming, Secretary of the Northern Territory Department of Health. The convener and invited chairman was Prof. John Cawte of The University of New South Wales, stationed at Prince Henry Hospital, Sydney, but a long-time outdweller visitor-researcher.

The Angurugu Council, Groote Eylandt, and the Groote Eylandt Mining Company kindly made relevant personnel available to attend this meeting and provided the fares of some contributors travelling from outside Darwin.

This meeting was not designed as a medical conference in its usual sense. Medical information about these disorders was not felt, as yet, to be complete enough to generate that. However, enough information was available in early 1987 to convince both Prof. Cawte and the leading field researcher, Dr Charles Kilburn, that an informal gathering should be convened to share this information and to discuss the growing concern about these unusual disorders and their possible chemical environmental associations. Prof. Cawte and Dr Kilburn considered that they might be held remiss if they did not convene such a meeting, even while the present information is more contributory than completed.

Speakers were invited from the involved groups, ranging from the sufferers and their affected community outwards to consultant chemists and doctors. Speakers were asked to present their information in brief commentaries. Time was allowed for audience questions, discussion and for future planning designed to understand and to counter these grave conditions.

The meeting was, in effect, a sequel to an initial gathering held to discuss the outset of this research program, convened at the N.T. Department of Health, Darwin, on 1st December 1983. That meeting, which was then deemed confidential, had been entitled: *Possible Association of Manganism with the Groote Eylandt Syndromes.*

At that inaugural 1983 meeting Prof. Cawte presented two papers before lunch :

1. *Manganic Syndromes : Neurological; Psychiatric; Teratological; others.* Discussion followed.

   Manganese Toxicology: Findings since 1975: Human; Veterinary; Marine-Biological. Discussion followed.

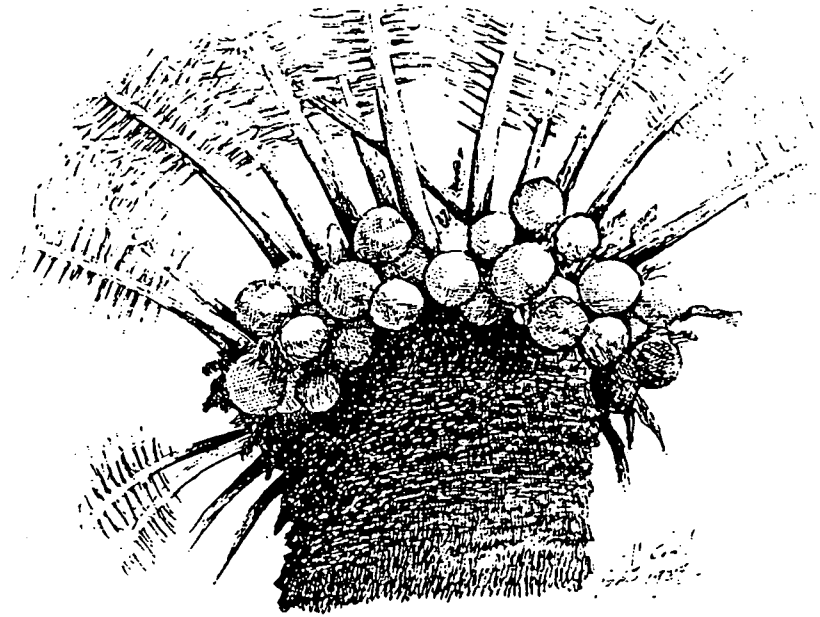
After lunch the research proposals were discussed in terms of the findings up to that time; of suggested future work; of costs; and sources of funds.

Immediately following that 1983 meeting, the Groote Eylandt Mining Company kindly donated $30,000 expense costs per year, for up to three years, and the Angurugu Community Council $10,000 per year, for up to three years. The former fund has been used chiefly for transport of skilled consultants to the distant site, and the latter chiefly for payments to local informants at the site helping the study.

Two years subsequently, in 1985, the NH&MRC awarded, on Prof.Cawte's application, a research fund that enabled Dr Charles Kilburn to undertake resident medical officer activity at Angurugu, Groote Eylandt, including a control study at Galiwinku, Elcho Island, N.T. Dr Kilburn also registered as a higher degree candidate at the University of New South Wales.

The present (1987) meeting was designed to review findings (especially clinical and chemical) since 1984, facilitated by the above financial support. The donors are thanked, together with members of the N.T. Department of Health and other organisations who have assisted. A tribute is paid to these parties in the Chairman's *Introduction of Participants* at this meeting.

After the June 11th 1987 colloquium, the contributing speakers were invited to draft their observations, which had been hastily prepared in most cases, in a form suitable for publication of *Interim Proceedings*, including their references. These papers were typed by Ms Mary Hammill, compositor for the two education journals funded by the Commonwealth Department of Aboriginal Affairs: *The Aboriginal Health Worker* (Hon. Editor, John Cawte) and *The Aboriginal Child at School* (Hon. Editor, Dawn Muir). The final collection of material was printed, for limited circulation, by the University of Queensland Printery, St Lucia, Brisbane, including line illustrations by Aboriginal medical illustrator, Billy Reid.



A Burrawang (Cycad) in fruit, Groote Eylandt

COLLOQUIUM OUTLINE

Changes in the order of speakers were made on the day, reflecting speaker availability and other factors arising at the time

Chairman:	Introduction of participants; apologies and some tributes.
Mr Murubuda Wurramarba:	Views of the Angurugu Community Council, from its Chairman.
Dr Joan Ridley:	A Neurological Ethnic-Geographic Isolate (read from clinical paper by Professors Leslie Kiloh and John Cawte - not published in Australia).
Mr Graham Hams:	Findings from the Clinical Chemistry Laboratory at the Prince of Wales Hospital, Randwick, Sydney.
Dr Mark Florence:	Findings concerning the Manganese Ecology at Angurugu, from CSIRO at Lucas Heights, Sydney.
Dr Charles Kilburn:	Pediatric and Other Disorders at Angurugu.
Professor John Cawte:	What One Patient Taught One Epidemiologist (illustrated by video tapes of this patient under treatment).
Professor David Turner:	Anthropological Concerns.
Professor John Cawte:	The Angurugu Syndrome: Should the Community Consider Relocation?
Afterwords for the Conference:	Press Release; Paper reports; Notes by the Hon. W.C. Wentworth; Reports from Hawaii, and others.

CHAIRMAN'S INTRODUCTION OF PARTICIPANTS

Ladies and Gentlemen

Thank you for coming to an unusual gathering. I turn to you especially, Dr Keith Fleming, for hosting us all in your capacity as Secretary for Health and a few other services. I turn to you, Dr Ella Stack, for arranging this meeting in the Blue Room of Health House, providing our morning and afternoon tea and lunch, along with your usual interest in health problems. This is not a medical conference, but an associates' sharing of findings so far made respecting the Angurugu syndromes. It's a difficult issue. Dr Charles Kilburn and I, as chief workers in the field, felt that if we did not now call a meeting, we could be criticised for failing to communicate a problem that is hard to counter, and one in which the usual solutions do not apply.

Today's program has been altered several times during the past week. Some speakers are out of Australia. I could not confer with Dr Kilburn because he was out of contact with Sydney, being on Elcho Island. There are deficiencies today but at least we can all share the major points. We can conduct a medical conference in two or three years, my own estimate of the time needed for a full account, given enough support and funding on the way.

First, some apologies. Our early clinical worker, Professor Leslie Kiloh is having his Festschrift in Sydney today. He wanted to come to Darwin but I persuaded him that he'd better stay at home on this occasion. Dr Bill Webster, our hardworking embryologist exposing gravid rats to manganese, is overseas. So is Dr Ivor Dreosti, the expert on manganese, alcohol and superoxide dismutase at Adelaide's CSIRO. Dr Kilburn and I have consulted him in his manganese studies, which I hope Dr Florence, of Sydney CSIRO, will mention today.

It was Mr Clyde Holding, the present Minister for Aboriginal Affairs, who suggested that I should convene this meeting. We are fortunate to have with us his distinguished predecessor, the first Minister for Aboriginal Affairs, Hon. W.C. ("Billy") Wentworth.

We are grateful that we have a representative group of our Angurugu friends, who first asked me to study this problem years ago. We conferred with many more of them on Groote Eylandt yesterday. Today their group is led by Mr Murubuda Wurramarba, the Chairman of Angurugu Community Council. Also present is the Town Clerk, Bobby Nungamudjba, who spoke on this subject in Canberra with me a month or two ago. My friend, patient and chief helper is here., I will dwell later on what he has taught me. I am delighted that my dear Damiya is here today. She is the senior of the female health workers at Angurugu. We visitors slept at the Health Centre last night, and helped Damiya during a night disturbed by ills ranging from infection to compound fracture of the ulna.

The N.T. Department of Health is, of course, well represented here. I'm most grateful for the response of the Secretary, Dr Keith Fleming, whose words by phone to me in Sydney linger firmly in my mind. He just told me, "I'll do anything I can to help in this matter." He has given us hospital accommodations, use of a hire car, and is even asking me to lecture on Pablo Picasso tonight at a small barbecue at his (Keith's) home. A masochist for punishment, obviously, Dr Fleming.

It is good once more to meet with some Territorian medical friends. I've known the work of Dr Kerry Kirke over many years in The Centre. He's here as Assistant Secretary for Health Advancement, with responsibilities for Aboriginal health. Dr John Hargrave and I must have had Christmas dinners together after all the Hansen's disease he managed, ten years in a row, at the home of Rev. Harold Shepherdson and his wife Ella, at Elcho Island. It is good to see here Professor John Mathews, of the Menzies School of Health Research, who has such responsibilities for the future of health here, and who takes a special interest in this study. Also Dr Joan Ridley, an old psychiatric colleague of Professor Kiloh (I believe another Northumbrian) and myself.

I had dinner with Mrs Margaret Sheridan at Gove two nights ago. It's good to see her here, as Regional Director of East Arnhem Health. I rarely come to Darwin nowadays since I receive such support from her and her predecessors in East Arnhem Land during my medical invitations by those communities. Margaret knows all the best places to eat in Gove,

I am deeply relieved to find that Dr Mark Florence, outstanding trace element expert from CSIRO, Lucas Heights, has made it today. CSIRO researchers know a lot more about minerals than do medicos, and Mark has some crucial findings to offer us today in two talks that he is offering on behalf of himself and his Adelaide CSIRO Colleague, Dr Ivor Dreosti. Indeed, without the CSIRO findings on manganic ambience at Angurugu, I doubt if we should be holding this meeting today. Our sincere medical thanks to CSIRO and Dr Florence.

I have been travelling in the company of an old friend, Mr Don O'Rourke, First Assistant Secretary of the Programs Policy Division of the Department of Aboriginal Affairs in Canberra. Don wanted to look at the patients of whom we speak in their home setting at Angurugu. So did our other travelling companion, Mr Peter Moyle, of the Aboriginal Health Branch of the Commonwealth Health Department in Canberra. The Angurugu people were pleased to greet them.

From the Church Missionary Society I bring you the good wishes of Bishop Clyde Wood, who has always been interested and will try to be here later today. Two C.M.S. workers of Angurugu deserve our special thanks. Mary Harris (Mrs Eves) cannot be here today, but it was chiefly her concern, as a social worker, that first attracted our attention to this illness, as Dr Ridley's opening paper will describe. Mr Lance Tremlett, as C.M.S. Manager at Angurugu, has given us endless support and encouragement and, with his wife Gwen, hospitality over many dinner tables. Only yesterday Lance was showing us the famous old Mission garden, which we now know to be saturated with manganese, along with its plants that the people ate so much in those days.

I feel bound to pay a tribute to the remarkable group of C.M.S. research missionaries at Angurugu who have helped us in our work - Judith Stokes, Julie Waddy and, most of all, Dulcie Levitt now retired in Sydney, a botanist who periodically visits me at my hospital to talk about plants and people of Groote Eylandt. Our findings could offer Dulcie a new chapter in the next edition:

We welcome some guests from the Groote Eylandt Mining Company Pty Ltd, led by the manager, Mr Sergio Fuenzalida who, after being operations superintendent succeeded the previous manager, Mr Trevor Tennant, who

provided us with financial help some years ago. The Company's speaker today is Mr Alan Wright, a public relations officer who has always been deeply interested in the Anindilyakwa people, many of whom have worked for the company. I also see Mr Clive Thurlway, who is responsible for environmental interests of the company, and others. All have been helpful to us. We don't see here a previous employee, Mr Jack O'Hare, who retired on the Eylandt down at Yimbagwa, in a caravan. Jack is in Casuarina Hospital having surgery for his hip. I'll call on him tomorrow. Jack is not only welcoming to me on my too rare visits, but full of information about early times. We value Jack and wish him successful recovery.

Of my B.H.P. colleagues, I particularly welcome on everybody's behalf, Dr Robert Hart, head of the Division of Health and Safety for that company. I have been seeing Bob on and off over the years and I have found him realistic and experienced. My only objection to him is that he lives in Melbourne, when he is not overseas as he often seems to be. I decided to go to Melbourne BHP headquarters to see him last week, as he was not able to keep his appointment to see me in Sydney. He is accompanied by his epidemiologist colleague, Dr Michael Fett.

From my own group of hospital consultants in Sydney we welcome the neuro-chemist, Graham Hams. Graham makes some striking discolosures today. With his newly installed atomic absorption spectrometer, he has disproved a contention that one commonly finds in older books, that tissue manganese is not measurable in humans, for the most part. Graham has demonstrated high levels in the blood of most of our neurological patients, which we never expected to find. It helps us!

Of my other colleagues, the neuro-pathologist, Prof Bruce Warren was here a month ago. As yet we have no autopsy studies but we hope that Bruce will rectify this. The community has accepted Bruce's role. The neurologist, Dr Keith Lethlean will be up here next month with his myogram recorder and assistant, Dr Heather Johnson.

I really want to thank all the nurses who have assisted us over the years, but there are too many, so I'll restrict my thanks to Rachel Jordan, one of the first sisters to help me ten years ago. I saw Rachel yesterday in her new capacity with the AIDS problem. We are all in her debt.

Groote Eylandt has known many famous anthropologists, from Norman Tindale, whom I knew of old at the South Australian Museum (whenever he was there) and C.P. Mountford. I suppose the most famous is Donald Thomson, whose remarkable public achievements one can read about in Dr Nicolas Petersen's well illustrated book, *Thomson in Arnhem Land*. Indeed, Thomson, more than any other, created precious Arnhem Land as a Reserve for its people. I have also met Prof Fred Rose, now in East Berlin, who had the foresight to include photographs of residents in his book. But today we are lucky to have with us the leading anthropologist of the present day, Prof David Turner of Toronto. He will be speaking to us shortly.

I have to apologise to my normal Arnhem Land hosts of Elcho Island, where I have spent most of my vacations for 20 years as an anthropologist physician. I have attended them medically and studied their healing and their mourning, as well as their religion, and their latest craze of drinking Kava from Fiji. I am involved in advising the Western Australian Government on that drug substance - we are convinced it is a drug, not a food - but I have had to sacrifice Elcho interests to attend to Groote Eylandt of recent years. I'll go back "home" when I can. Meantime, our child specialist who is working on Groote under my NH&MRC grant, Dr Charles Kilburn, recently carried out his control study on Elcho, and no doubt represented me well. You'll hear today how we are lucky to have such a sincere and balanced specialist as Dr Kilburn. I'm grateful that he'll move to Darwin after the grant is over and hopefully continue his work on Groote Eylandt as a consultant.

Giving my grateful thanks to you all for contributing today, I can only apologise if I have missed someone I should recall. You are all deeply valued in the pursuit of this mysterious and tragic disease and the unusual ambience in which it occurs.

A final word for the most valuable consultant who is not here today, because he is at home in Quebec. Professor John Donaldson is in my opinion the world's authority on the effects of manganese on the nervous system. He visited me last year when I was a guest at the Center for Advanced Study in the Behavioral Sciences at Stanford, California, and he taught me and Dr Kilburn last December in Australia about the vagaries of this element in the nervous system. We await his new article on this subject in the forthcoming issue of *Neurotoxicology*. We wish you were here today, John, to talk about the 140° longitude neurological disorders.

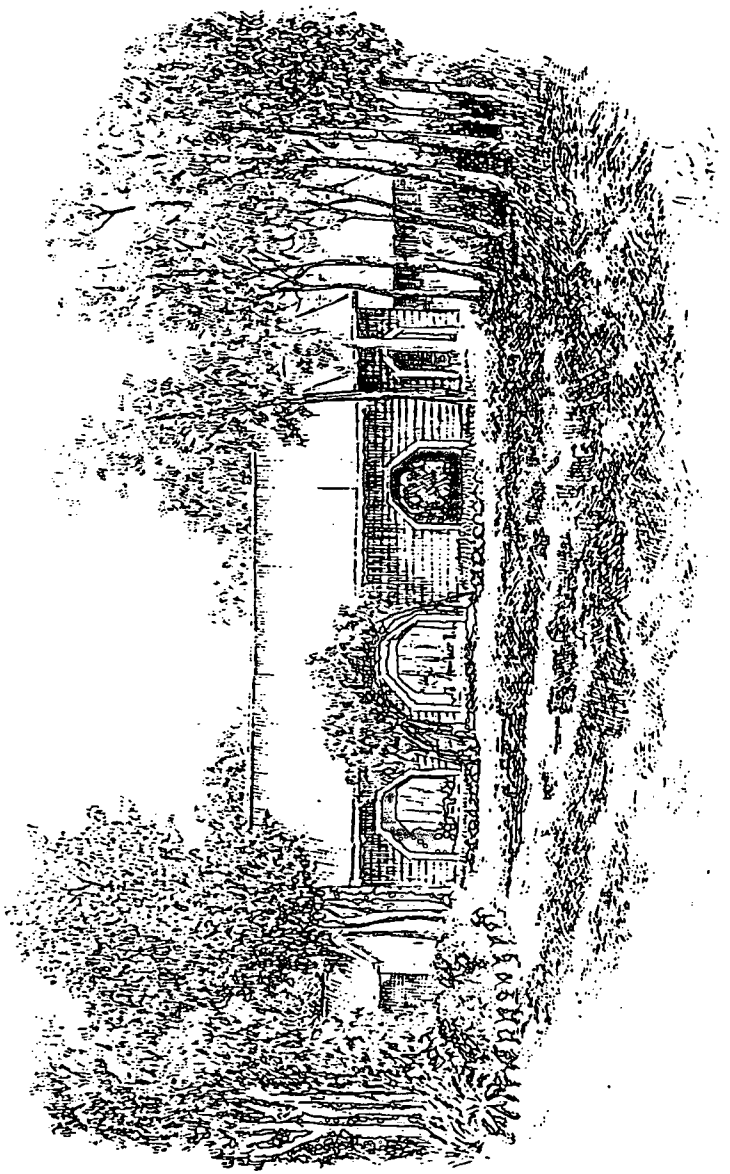
CHAIRMAN, ANGURUGU COUNCIL

Mr Murabuda Wurramarba, Chairman of Angurugu Council, spoke briefly about the concern of his people over their strange diseases. He mentioned that they had asked Dr Cawte to give his opinion some years ago. Since then many advisers had visited. Finally Dr Charles Kilburn who had lived with them and carried out important medical work, particularly with children.

Mr Murabuda said that his people were anxious that the research go forward to a successful conclusion. The disease must be controlled to make the people strong and happy. He emphasized that the people did not want any public attention, fuss or trouble. They just wanted their disease understood and relieved.

He thanked today's experts for coming to this meeting.

A Groote Eylandt shoreline



The church of the Church Missionary Society, at Angurugu.

A NEUROLOGICAL ETHNIC-GEOGRAPHIC ISOLATE ON GROOTE EYLANDT°

L.G. Kiloh and J.E. Cawte#
University of New South Wales

Groote Eylandt, which curiously retains its Dutch name though probably discovered by the Portuguese, is the largest island in the Gulf of Carpentaria in the North of Australia. Its bearings are latitude 14° South and longitude 138° East. Together with a small cluster of Aborigines on one of the nearby islands and on the mainland, the total Aboriginal population is about 1100.

On our way back from Elcho Island we visited Groote Eylandt briefly in 1977 and met Mary Harris, a social worker who had spent a number of years on the island. Mary Harris was disturbed by the number of Aborigines with neurological disorders and drew our attention to them. In the short time available we saw a number of the patients and returned a year later accompanied by Dr Keith Lethlean and Dr Graeme Morgan. With the help of Mary Harris and the nursing sisters we were able to identify thirteen definite and three probable cases. We studied them in more detail than was possible during our earlier hurried visit and gave some consideration to possible etiological factors.

To summarise the first findings (Kiloh *et al.* 1980) there were seven cases showing features of a motor neurone disease, two with only lower motor neurone involvement and five with the additional lateral sclerosis. One of the latter had shown only lower motor abnormalities on our first visit. In four of these seven cases abnormalities were observed by the mothers soon after birth. Most of these patients also showed a striking degree of hypotonicity with very lax ligaments. One of this group whom we did not see had died several years before, having developed a bulbar palsy. There were six patients with a curious mixed picture showing cerebellar features and pyramidal tract involvement. Four showed a variety of supranuclear and internuclear ophthalmological paralyses and three some muscle wasting. In addition, there were three

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°From K.M.Chen & Y.Yase (Eds) 1984: *Amyotrophic Lateral Sclerosis in Asia and Oceania*. National Taiwan University.

#This paper was read at the Conference by the Darwin psychiatrist, and colleague of the writers, Dr Joan Ridley.

Aborigines with lax ligaments whom we thought had a mild and probably non-progressive ALS-type syndrome. Of thirteen definite cases, one showed a mild dementia and in another this diagnosis was queried. A mild degree of parkinsonism was also queried in two patients.

It is unfortunate that we have had great difficulty in obtaining funds to investigate the Groote Eylandt population further. One of us (J.E.C.) has managed to look in briefly several times on his journeys to and from Elcho Island. We have kept in close touch with one of the important members of the Aboriginal Council who happens to be one of the patients. About two thirds of the cases appear to have progressed. Two have died, but even had we been there at the time it would probably have been impossible to have obtained autopsy material. One new case has been located with cerebellar and upper motor neurone features.

It might be worth adding that other peculiarities have been noted in the Groote Eylandt inhabitants. In one family ten of twelve siblings have died, nine in early childhood. One, who survived to the age of five years was never able to walk. In two other related families there is a remarkably high incidence of heart and renal disease and of twelve siblings, four have died in late adolescence or early adult life and two others are affected. There is also hearsay evidence of a psychiatric syndrome unusual in Australian Aborigines, in which the patient is subject to unexpected episodes of rage and aggression - something between amok and the episodic dyscontrol syndrome. Our informants indicate that in women it occurs in the first trimester of pregnancy.

We considered that the syndromes, although varying widely, were likely to be examples of a polymorphous condition having a common etiology.

At the time of our first visit we were impressed by the strong familial nature of the illnesses and we thought that they were likely to be genetic. In a small closed community of this kind everyone is related in some degree to everyone else and Dr Graeme Morgan found great difficulty with his genetic studies. However, strongly against a primary genetic basis was the fact that in the 1920s the population of Groote Eylandt had been studied separately by Dr Tindale and Dr Rose, both of them competent and observant anthropologists. Neither of them referred to any neurological disease. Rose photographed every member of the population but his findings

were not published until 1960; no indication of these disabilities appears. Furthermore, none of the missionaries drew attention to the condition, nor do the Aborigines themselves have any tradition - and established sorcery explanations - of such a disorder.

The possibility that neurotoxins derived from cycad nuts or cassava was considered but rejected. The most striking ecological feature of the population of Groote Eylandt is that most of them live in the middle of a large manganese deposit and are surrounded by open cut mining activities and dumps of crushed ore. In the principal of their two villages, lumps of black manganese oxide can be picked up in the streets and at any time a thin film of black dust can be wiped from furniture and other exposed objects. The local river from which the water supply is derived runs across a bed of exposed manganese ore. The other Aboriginal village in which two cases were identified lies on the opposite side of the island and has no nearby manganese deposits. However, there is much movement between the two areas. The three mainland patients are also distant from the major manganese deposit but again mobility does occur and furthermore they live on the edge of Blue Mud Bay, originally so named by Flinders, Captain Cook's successor as a cartographer. The colour was later found to be due to manganese. Amongst Aboriginal bark paintings those from Groote Eylandt can easily be identified at a distance by their extensive use of black pigment - a colour available to other Aboriginal communities only as charcoal.

At the time of our visit we considered the possibility that manganese was responsible for the genesis of the neurological abnormalities. At that time our knowledge of manganese intoxication was limited to the acute and chronic syndromes suffered by miners in Egypt and Chile, which are dominated by extrapyramidal syndromes. These differ markedly from from those presented by the Groote Eylandt Aborigines. At the same time, we did not overlook the fact that up till 1942 the entire population lived beside Emerald River some 20 odd miles south of the manganese deposit. In that year their airstrip assumed strategic importance and was taken over by the Royal Australian Air Force. Perhaps not without justification, the community became concerned and moved the settlement up the coast to the next major water supply and established the village of Angurugu where most of our cases were found.

It is interesting to consider the birth dates and the times of onset of the sydnromes in relation to the move to Angurugu. Of the sixteen cases, five were born before the move and only two after the development of the mining operation. In none of the cases we know about did the syndrome appear before the move but in eight the symptoms began before the mine was opened.

We have carried out an intensive study of the literature on manganese and there appears to be considerable evidence from animal and veterinary studies that in addition to its effects upon the mature nervous system, manganese is capable of teratogenic effects perhaps directly, perhaps by interaction with other elements, or perhaps in association with protein malnutrition.

[Our early notes on these syndromes were made nearly ten years ago. Since then we have published several research papers describing our studies and we have established a research physician on the island. The recent findings of high levels of manganese in the blood of neurological patients and in the garden soil and plants of the village, will be outlined in today's proceedings. These findings certainly add interest to our early investigation].

REFERENCES

Kiloh L.G., Lethlean A.K., Morgan G., Caute J.E., Harris M.: An endemic neurological disorder in tribal Australian Aborigines. *Jnl Neurol. Neurosurg. Psychiat.* 1980:43, 661-668.

ANALYSIS OF MANGANESE IN WHOLE BLOOD

Graham A.Hams Trace Metal Laboratory
Division of Clinical Chemistry
Prince of Wales Hospital
RANDWICK NSW 2031.

A method for determining the concentration of manganese in whole blood was established in my laboratory during 1986.

The method utilised the laboratories' AA975 atomic absorption spectrometer which was equipped with the GTA 95 electrothermal atomiser (both manufactured by Varian Pty.Ltd. Mulgrave, Vic.) The analytical technique was a novel application based on a technique reported in literature in 1986.(1)

The spectrometer was operated in double beam mode and used a deuterium background correction facility. The furnace atomiser employed a solid pyrolytic graphite platform to reduce condensed phase matrix interference.

Samples for analysis were collected on Groote Eylandt by Charles Kilburn, as heparinised whole blood. The collection apparatus was 'rinsed' with patients blood prior to sampling for manganese so as to minimise contamination from the hypodermic needle. The samples were transported to the laboratory at 4°celsius.

Within the laboratory, the samples were diluted to one fifth of their original concentration with manganese free diluent water. The diluted blood was mixed with a small volume of 70% w/w nitric acid (Univar, Ajax Chemical, NSW) and more water within the furnace atomiser. The temperature of the atomiser was increased slowly from 40°celsius to 400°celsius while maintaining a pure oxygen atmosphere over the sample. The atomiser temperature was then increased more rapidly to 800°celsius after changing the atmosphere to pure argon. Gas flow was stopped and the sample residue atomised at 2600°celsius. Atomic absorbance signals were measured as peak height.

The analysis was routinely calibrated with aqueous standards Periodically, the parity between aqueous calibration and standard additions calibration on a low manganese concentration whole blood was ascertained.

The analysis showed ample sensitivity. Peak height absorbances ranged from 0.04 units to 0.12 units over the laboratory reference interval of 100 to 350 nanomoles manganese per litre of blood. This interval compares favourably with other workers' estimations of a reference interval (2,3,4.)

Background absorption during atomisation of whole blood samples can be an intractable problem. The combination of matrix modification, oxygen ashing and temperature profile used in this analysis both reduced the absolute size of the background signal to a manageable level and moved it temporally so that interference was minimised before the application of background correction. (fig.1)

Analysis of whole blood collected from eight neurologically affected Aboriginals from Groote Eylandt showed six individuals to have markedly increased manganese concentrations. Eight unaffected Aboriginals resident in the same area showed normal blood manganese concentrations (5).

DISCUSSION OF THE RESULTS

The technique as applied appears to indicate a possible association between elevated blood manganese and the occurence of the "Groote Eylandt Syndrome".

If the association is shown to be valid by further testing it maybe that these affected individuals have increased organ exposure to manganese through one or a combination of the following metabolic abnormalities:-

1) increased intestinal absorption of a normal manganese load
2) increased exposure to environmental manganese but a normal uptake.
3) decreased hepatic excretion of manganese

Future studies to verify or reject the association between elevated blood manganese and the neurological syndrome should include:-

1) some form of population survey or surveys of Groote Eylandt to accurately determine the local "normal" range of whole blood manganese levels.
2) comparison of results for affected and unaffected individuals to check for the association.
3) follow-up studies over a period of some months to identify varying exposure to manganese.
4) analysis of cord blood to determine the extent of in utero exposure.
5) manganese body balance studies

CONCLUSION

A method for analysing manganese in whole blood samples by atomic absorption spectrometry has been developed. The technique has good operational characteristics and shows excellent analyte and background signal separation.

Application of the method to a small sample of bloods taken from Groote Eylandt Aboriginals may indicate some association between elevated blood manganese and a neurological syndrome. This association has yet to be proved

Future studies should include a population survey to assess general exposure and individual response to environmental manganese.

It should be noted that this laboratory is able to carry out a small scale preliminary survey for no charge. However, should larger scale surveys or population monitoring be required (either by the Aboriginal community or by the Groote Eylandt Mining Company for its employees) some funding would be required to increase the laboratories analytical capacity.

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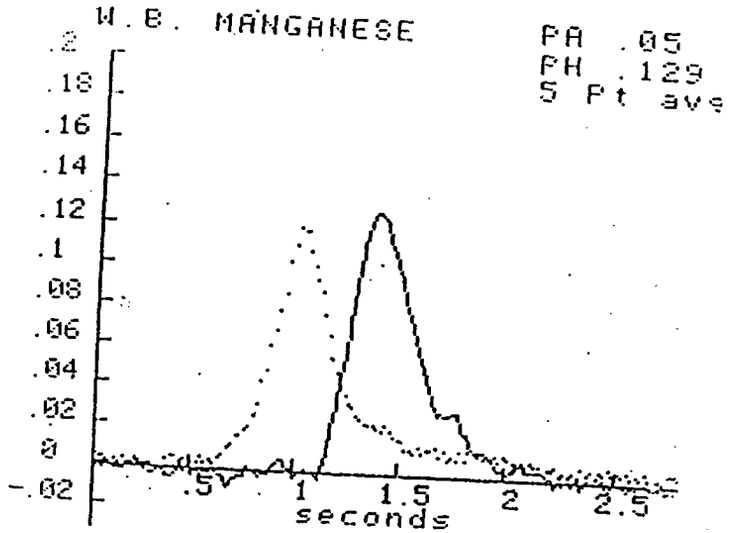
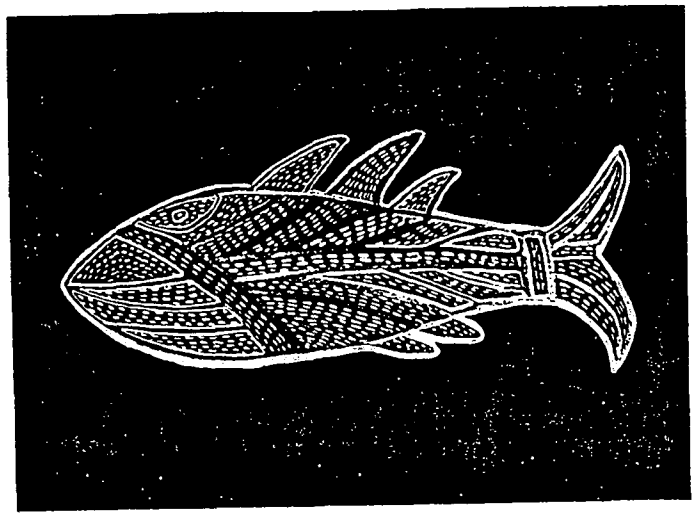


Fig.1 Detail of analyte (dark) and background (dotted) signals during the atomisation phase of the blood manganese analysis. The sample concentration was approxomately 300 nanomedes per litre.



The Barramundi
by
Kneepad
From *Time Before Morning* by Louis Allen, 1975.
Crowell Co., New York.
The Groote Eylandt style often features prominent figures in dashed lines on a background made black by manganese oxide rather than by charcoal.

Ecological Studies of Manganese on Groote Eylandt

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1. Introduction

Most manganese salts have low acute toxicity, and manganese was thought for a long time to be one of the most innocuous of elements [1]. The long-term (chronic) toxicity of manganese was recognized later, as a result of neurological disorders with symptoms similar to Parkinson's Disease appearing in some manganese miners, particularly those in Chile [2].

Groote Eylandt has extensive and rich manganese deposits which are mined and provide a valuable export for Australia. The main Aboriginal village of Angurugu is situated in one area of manganese mineralization, with high soil and plant manganese. A small number of Aborigines have developed unusual neurological problems which are somewhat similar to those reported for miners suffering from manganese intoxication, and it was important to determine if these problems (the "Angurugu Syndrome") were associated with excessive manganese intake.

In this respect, an obvious question is: "If all the inhabitants of Angurugu are uniformly exposed to high levels of manganese, why are only 1-2% of the population affected?" This question can be answered on the basis of individual susceptibility. In the Chilean manganese mines, less than 5% of the miners developed chronic manganese toxicity; one miner may have been severely affected while his workmate, working beside him for the

some length of time, and exposed to the same concentrations of manganese in air, showed no toxic symptoms whatsoever [3]. This phenomenon of individual susceptibility has been observed with other metals such as lead, mercury and beryllium, and also with tobacco smoking. Most people know of a relative or friend who has smoked heavily all his life yet has not developed lung cancer or any of the other smoking-related diseases. Others, with a much lower tobacco usage, succumb quickly. The differences in ability to cope with toxicants is believed to result from individual variations in uptake rate and clearance rate of the toxicant, and the inducibility of enzyme systems which detoxify the foreign compound. In case of manganese, the most important factor is believed [4] to be the differences in the excretion ability of the liver and kidneys.

This study was undertaken to establish manganese concentrations in the environment and diet of Groote Eylandt Aborigines, and to compare the results with world average concentrations.

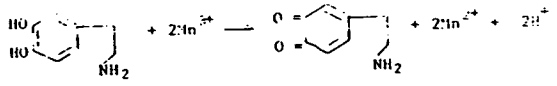
2. Toxicology of Manganese

Donaldson and co-workers [5] have shown how the neurotoxicity of manganese could arise as the result of Mn(II)/Mn(III) catalysis of dopamine oxidation in the brain. Our own studies at Lucas Heights indicate that the relevant reactions are:

$$Mn^{2+} + O_2^{\cdot} \longrightarrow Mn^{3+} + O_2^{\cdot -} \qquad (1)$$

$$Mn^{2+} + O_2^{\cdot -} + 2H^{+} \longrightarrow Mn^{3+} + H_2O_2 \qquad (2)$$

$$\text{net, (1) + (2): } 2Mn^{2+} + O_2 + 2H^{+} \longrightarrow 2Mn^{3+} + H_2O_2 \qquad (3)$$



(4)

dopamine — dopamine quinone

Reaction (1) proceeds only in the presence of a manganese(III)-complexing ligand (such as pyrophosphate, citrate or xanthine) and dopamine. The products of manganese and dopamine oxidation, ie, hydrogen peroxide and dopamine quinone, are strongly neutrotoxic. Catalase, the enzyme responsible for destroying H_2O_2 is low in the brain, and superoxide dismutase, the enzyme which dissociates superoxide radical ($O_2^{\cdot -}$), is unevenly distributed [6]. Manganese(II), however, efficiently catalyzes the dissociation of $O_2^{\cdot -}$. Superoxide radical, normally considered a dangerous species in biological systems, is nevertheless essential in the brain for the synthesis of the neutrotransmitters, norepinephrine and serotonin [7]. A certain level of manganese may also be essential to participate in vital redox reactions, but too high a concentration could lead to serious toxic effects.

The neurotoxic effects of excess manganese may be, (i) reduction of dopamine concentrations, (ii) production of toxic dopamine oxidation products (quinones and semi-quinones), (iii) production of hydrogen peroxide (iv) destruction of superoxide radical. Other metal ions, such as Cu^{2+} and Fe^{2+}, can also catalyze these reactions, but they are usually tightly bound in enzymes, and not free to participate in reactions such as (1)-(4).

3. Blood Analyses

The determination of manganese in blood is of little use for the diagnosis of chronic manganese poisoning [3]. Manganese miners with severe symptoms of manganism, after removal from the workplace, usually had normal manganese-in-blood concentrations [3]. On the other hand, apparently healthy miners, working in the mine, had high blood manganese. Manganese in the human body is characterized by two half-lives of 4 and 40 days, so blood manganese can only give an indication of recent exposure, and provides no information about the body store of manganese [2]. Nevertheless, for equally exposed individuals, high blood manganese may

indicate those with enhanced uptake mechanisms and/or deficient clearance mechanisms.

Results for catheter-collected (Jan 1987) blood from Groote Eylandt inhabitants are given in Table 1. The manganese values were determined by Mr Graham Hams, Clinical Chemistry Department, Prince of Wales Hospital. Neutron activation analysis was also carried out at Lucas Heights on some of the bloods and, in general, good agreement was obtained.

The average blood manganese (µg/L) for the four groups (Table 1) were: GEMCO workers (omitting No. 1), 8.4; Caucasians in Angurugu, 7.3; affected Aborigines (omitting No. 7), 36.1; unaffected Aborigines, 18.9. The normal range for manganese in blood is 6 to 12 µg/L, with a mean (Sydney) of about 8.5 µgMn/L. The Caucasian inhabitants of Groote Eylandt have blood manganese values close to this mean, but Aborigines unaffected by the Angurugu Syndrome have double the Caucasian blood manganese, and those affected, four times. The affected Aborigines also had low hemoglobin (normal range 12-18 g/dL) and low ferritin (normal 25-150(F), 75-260(M) µg/L). Therefore, in addition to high blood manganese, they have a low iron status (anemia).

One sample of cord blood from an Angurugu baby delivered in Gove had 41 µgMn/L, even though the mother's blood was normal (7.2 µgMn/L) and the concentration of manganese in the placenta was low (0.12 µg/g dry wt.).

4. Factors that Exacerbate Manganese Toxicity

The following factors are known to increase the toxic effects of manganese [8].

(a) Low iron(anemia). Iron and manganese have a similar uptake mechanism; anemic individuals have enhanced absorption of both iron and manganese, and are known to be more susceptible to the toxic effects of this element [2].

(b) Chronic infections. Infections cause an increase in the production of H_2O_2 and free radicals in the body, putting greater strains on the ability of the cellular and extracellular antioxidants to scavenge these toxic substances, already produced in excess by the catalytic action of excess manganese. Some natural antioxidants are vitamins C and E, glutathione and free radical-dissociating enzymes.

(c) High alcohol intake. The catabolism of ethanol liberates H_2O_2 and free radicals, and depletes the liver of the antioxidant glutathione.

(d) Low dietary calcium. Manganese can displace calcium from nerve endings and hence disrupt the central nervous system. This is more likely to happen in an individual with high manganese and low calcium status.

(e) Low zinc status. Zinc protects sulfhydryl groups (e.g., glutathione) from oxidation by H_2O_2 and free radicals. These compounds are therefore more susceptible to manganese toxicity when zinc is depleted.

5. Manganese in sweat and urine

Three Aboriginal brothers from Angurugu, one deemed as severely affected by the Angurugu Syndrome, one moderately affected, and one unaffected, were brought to Sydney for medical tests. In all three cases, the urine (<0.3-1.1 µgMn/g creatinine) and sauna sweat (3-11 µgMn/L) were within the range found for Lucas Heights controls.

6. Chelation Therapy

The three brothers mentioned above were treated at Prince Henry Hospital with calcium ethylenediaminetetraacetic acid (EDTA) in an attempt to remove excess body manganese. Urine analysis showed, however, that after correction for the manganese blank in the Ca-EDTA, no manganese was removed by the chelation therapy.

7. Manganese in hair

Hair concentrates trace elements from blood supplying the hair follicle, and hence manganese in hair should be an indicator of blood levels of this element. In addition, since scalp hair grows at the rate of 1.0-1.5 cm/month, changes along the length of a hair should be a record of changing blood concentrations during that period.

This ideal situation is complicated by external contamination of the hair - from dust, shampoos, and hair treatment which may add or subtract elements from the hair. Manganese is one of a group of elements known to increase along the length of a hair even when blood concentration of the element is constant. This was believed to be due to increased environmental exposure to the element as the hair grew, but our research has shown that the increase results from sweat elution. Sweat glands near the hair root produce sweat which travels up the hair, dissolving manganese from dust particles on the hair, and concentrating the element towards the tip of the hair. Under these conditions, hair is acting as a wick or chromatographic column, with sweat as the eluant. This phenomenon occurs only with those elements that form lipid-soluble complexes with sweat. To overcome this exogenous effect, a plot of manganese concentration in washed hair versus length from scalp was constructed for each hair sample, and the graph extrapolated to zero length. This "zero-length" manganese concentration should represent the hair manganese unaffected by external factors.

A summary of results is shown in Table 2. All Groote Eylandt inhabitants had hair manganese values higher than Sydney residents, probably as a result of a continuous, albeit low, intake of excess manganese. Aborigines had much higher manganese in hair than Caucasians, although there was no significant difference between affected and unaffected subjects.

8. Manganese in Air and Water

Manganese in air in Angurugu (average about 5 $\mu gMn/m^3$) is 100 x the Sydney and European average (Table 3). However, manganese in air would contribute only about 0.1 mg manganese/day to the intake of an Angurugu resident, and so would be an insignificant percentage of total intake unless, of course, respired manganese is particularly toxic. Manganese in Angurugu air is well below the occupational limit of 200 $\mu g/m^3$.

Manganese in the village tapwater and the Angurugu River appears to vary seasonally, up to 10 x the Sydney and world average. However, manganese from this source would amount to, at the most, 0.3 mgMn/day, and so would be insignificant. Calcium in the Angurugu River (0.2 mg/L) was very low, only 0.01 x world average.

9. Manganese in Traditional Food Sources

Some traditional ("bush tucker") food samples were collected from the Angurugu old village garden areas (used extensively before 1970) and analyzed for manganese (Table 4). Some of the foods were exceptionally high in manganese, and contained 3-100 x the world average for these items. A peeled yam, for example, had 660 $\mu gMn/g$ (fresh weight), compared with 5 $\mu gMn/g$ in a Sydney carrot. On this basis, one 20-g yam would supply 13 mg of manganese, or 3 x the recommended daily allowance (RDA) of this element (4 mg).

Boiled ("billy") tea extracts about 5 times the amount of manganese from tea leaves as does brewed tea. One litre of billy tea would contain 6-7 mg manganese.

10. Manganese in Soils

Soil samples in the old Angurugu garden areas (Table 5) were exceptionally high in manganese (up to 100 x world average) and very low in calcium (0.04 world average). Soil samples taken near Aboriginal houses in Angurugu were about 10 x world average in manganese. Umbakumba soil was very low in manganese.

11. Manganese in Organs of Experimental Animals

Organs of animals captured near Angurugu varied considerably in manganese content, but some were particularly high, e.g., thymus, adrenals, spleen, and the brain (Table 6).

12. Conclusions

I have reached the following preliminary conclusions from these

...

1. Angurugu Aborigines have a high intake of manganese, but the actual amount is very difficult to determine. Air and water contribute insignificantly to their total intake but, because of their "close to the earth" living, relatively poor hygiene, and the high manganese content of Angurugu soils, ingested manganese may be considerable.

2. Before the store was opened in 1970, Angurugu Aborigines used about 80% "bush tucker" in their diet. This bush tucker consisted largely of vegetables and fruit grown in the garden area, which has extremely high soil manganese. Their dietary manganese from this source alone could easily have been 100-200 mg manganese/day (25-50 x RDA). At present, bush tucker constitutes only 10-20% of their diet, and may not be as significant as damper cooked in the earth and billy tea.

3. There is no known way of measuring, in vivo, the total body burden of manganese. Blood and hair only indicate manganese in readily exchangeable pools such as soft tissue, and chelation therapy appears to be ineffective. The availability of autopsy samples would help considerably.

4. Anemia, chronic infections, high alcohol intake, low dietary calcium, and low zinc status are factors that exacerbate manganese toxicity, and are commonly found in Angurugu Aborigines.

5. Hair analysis suggests that Caucasians in Angurugu, and GEMCO workers, have a higher manganese intake than non-exposed persons, but much less than the Aborigines.

13. Future Work

I believe that the following work is necessary to clarify the question of excessive manganese exposure in Angurugu.

1. Additional blood analysis. Although it is well established that blood manganese analyses indicate only very recent exposure, they may pinpoint individuals with a defective clearance mechanism and/or enhanced uptake mechanism. Every attempt should be made to collect cord blood and hair manganese is concentrated across the placenta. Control cord blood samples would also have to be collected because little is known about the normal manganese concentration in cord blood.

2. Autopsy samples can be rapidly and non-destructively analyzed by neutron activation analysis. As many as possible should be collected.

3. An attempt should be made to estimate the bioavailability of manganese in Angurugu soils. Standard procedures could be used for this.

4. Hair analyses of people who have lived on Groote Eylandt and left should be carried out to determine if, and how rapidly, manganese in hair decreases when exposure to this element is removed. If levels remain high, it may mean that hair can be used as index of body burden of this element.

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TABLE 1 BLOOD ANALYSES ON GROOTE EYLANDT INHABITANTS

Subject	Mn µg/L	Fe µg/L	Hb g/dL	Ferritin µg/L
1. GEMCO workers				
1	22.3	503	16.6	233
2	6.0	454	15.5	280
3	9.9	420	14.2	124
4	9.1	407	14.9	146
5	12.6	498	16.1	165
6(F)	10.7	364	13.3	87
7(F)	6.9	406	14.5	158
8	6.3	495	16.8	93
9(F)	7.7	391	14.1	53
10	6.3	448	15.9	125
2. Caucasians in Angurugu				
1(F)	5.8	419	13.8	-
2	4.9	413	15.1	110
3(F)	8.8	361	12.1	30
4(F)	9.6	359	12.7	67
3. Affected Aborigines				
1(F)	38.7	331	11.3	28
2(F)	36.3	297	10.4	5
3(F)	15.7	356	11.4	0.3
4	42.3	191	8.9	11
5	42.1	-	-	-
6	41.2	-	-	-
7(F)*	9.3	381	13.1	367
4. Unaffected Aborigines				
1(F)	25.5	351	-	-
2	9.9	472	16.4	354
3(F)	16.8	336	12.3	34
4	17.6	453	15.0	96
5	24.9	-	-	-

*Lived in Umbakumba for 15 years.

TABLE 2 MANGANESE IN HAIR

Subjects	Mean manganese, µg/g	
	Scalp*	Pubic
Sydney	0.5±0.2	1.3±0.5
GEMCO workers	2.2±0.8	3.0±0.4
Caucasians in Angurugu	2.5±0.7	7.9±4.1
Unaffected aborigines	15±5	21±5
Affected aborigines	9±3	23±7

*Extrapolated to zero length.

TABLE 3 MANGANESE IN AIR AND WATER

Sample	Angurugu	Sydney	World Average
Tapwater, µgMn/L	4.3(8/85) 70(1/87)	5.8	-
Angurugu River, µgMn/L	27(8/85) 97(1/87)	-	8(for rivers)
Air, µgMn/m^3	23(3 m from road) 0.05 1.2(10 m from road)		0.04(European)

TABLE 4 MANGANESE IN TRADITIONAL FOOD SOURCES COLLECTED FROM OLD GARDEN AREAS*

Sample	µgMn/g fresh weight	
	Angurugu	Sydney
Fish, Angurugu River	36	0.3
Oysters, Mud Cod Bay	0.25	0.05
Yam, young	657	5**
Yam, old	484	5**
Citrus fruit	0.85	0.3
Banana	79	1.5
Billy tea	6.7	-

*U.S. intake: range 2-9 mgMn/day, mean, 3.7 mg/day.
**Root vegetables.

TABLE 5 MANGANESE IN SOILS

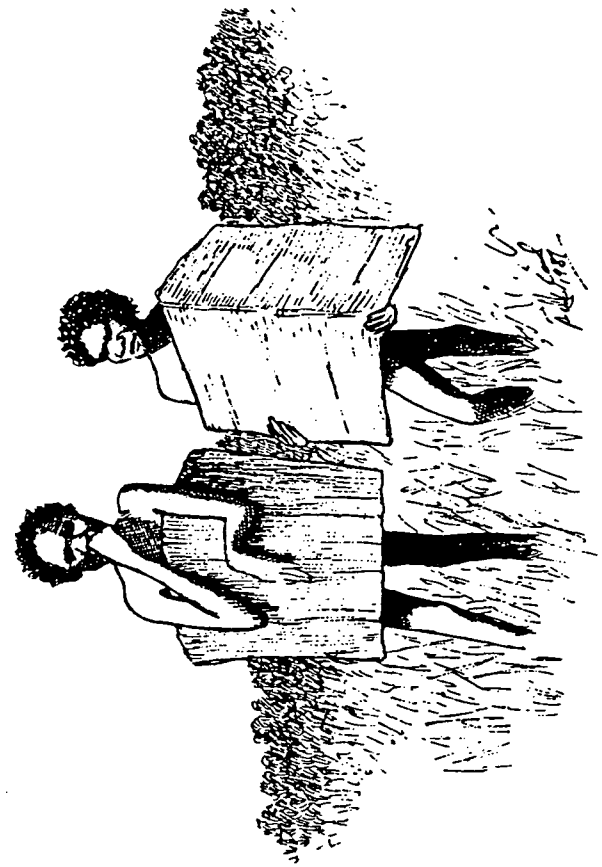
Source	Manganese, % dry weight*
Near Angurugu houses	0.2-1.2
Angurugu road	4.1
Old orchard	1.4
Old vegetable garden	4.6
Cassava plantation	0.11
Banana plantation	4.2
Mud Cod Bay sediment	0.33
Emerald River settlement	0.15
Umbakumba	0.002

*World average soil has 0.05% manganese.

TABLE 6 MANGANESE IN ORGANS OF EXPERIMENTAL ANIMALS

Organ	Manganese, µg/g, fresh weight			
	Angurugu Melomys*	Sydney rat	Groote dog	Sydney dog
Thymus	2.5	0.24	-	0.49
Adrenals	4.2	-	0.17	0.05
Spleen	1.7	0.24	0.27	0.33
Cerebellum	1.1	0.45	1.4	0.50
Choroid plexus	1.5	0.59	8.1	0.90

*Bush rat.



Early contact at the Mission. The deformity of the arm and hand of the woman on the left is particularly evident in the photograph from which Billy Reid worked - (Cole, K., 1975: *Groote Eylandt*, p.15).

NEUROLOGICAL DISORDERS ON GROOTE EYLANDT

Dr Charles Kilburn*

Unusual and poorly explained neurological disorders affect between one and two percent of the Aboriginal population of Groote Eylandt. Congenital malformations and psychiatric disturbances have also been linked to these Groote Eylandt syndromes (Cawte 1984) Rich manganese deposits in and around the main Aboriginal settlement of Angurugu have led to speculation about the possible role of manganese in these disorders.

For the past two years I have been resident on Groote Eylandt, employed by the University of New South Wales under a National Health and Medical Research Council grant to investigate these conditions. This research has been in conjunction with laboratory studies carried out by Dr Mark Florence of the C.S.I.R.O. at Lucas Heights Sydney, Dr William Webster at Sydney University and latterly Graham Hams at Prince of Wales Hospital Sydney. Professor John Cawte was responsible for instigating and coordinating this research.

Firstly I would like to discuss some results pertaining to birth defects, then to describe the neurological illnesses and finally to discuss some recent blood manganese findings.

In an effort to determine if there is an increase in congenital malformations I reviewed the birth records of all children born to Aboriginal parents resident on Groote Eylandt from the first of January 1975 till the first of January 1985. This cohort was also physically examined as part of a population survey. Another Aboriginal community was studied in the same way as a control group. There was no significant difference in either the incidence or the spectrum of of congenital malformations found. The incidence of stillbirths was also studied with the rationale that stillbirths may represent the severe end of a spectrum of teratogenic effects. These statistics were obtained retrospectively from local health centre records and community census information. Data were cross checked against hospital records. While cross checking is not fully completed, the incidence of Groote Eylandt stillbirths, 12 in a total of 286 births both live and stillborn, is not significantly higher than the 19 in a total of 579 of the control group. The general health status of these two communities was comparable, as evidenced by similar infant mortality rates (40 per 1000 Groote Eylandt; 39 per 1000 control). This should control for the effects of general health on the incidence of stillbirths and congenital malformations.

Next I would like to describe the neurological illnesses unusual to Groote Eylandt. My enquiry into the neurological status of the Groote Eylandt Aborigines has proceeded along two lines: an examination of affected individuals and a comprehensive survey of the childhood population.

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Aboriginal children born since 1/1/75 have been neurodevelopmentally assessed coincident with the community survey for birth defects. Since the Groote Eylandt Aborigines are in many respects still tribal and have had limited contact with the outside world until relatively recently, any discussion of these results requires a socially and culturally appropriate control group study for comparison. I have just finished an examination of such a control group but have not completed analysing the data. Therefore I will confine myself to a description of affected individuals.

Informants drawn from both Aboriginal and European sections of the community.were asked to list people with problems of weakness, gait, coordination and ocular movements. These are the major manifestations of the Groote Eylandt disorder being studied. After physical examination and study of their medical records those individuals whose disorders were explicable by other diagnoses (e.g. cerebrovascular accident, cerebral palsy, trauma, etc) were eliminated. This left a group of patients most of whom segregated readily into two clinical syndromes. This group includes most of the patients described by Kiloh *et al* 1980).

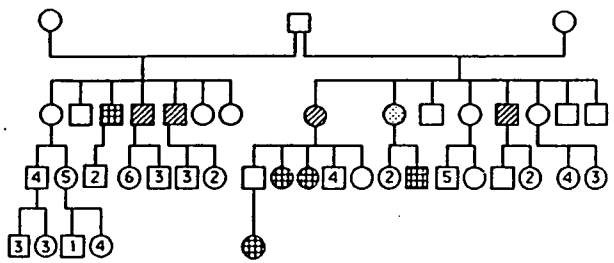
One patient, an Angurugu inhabitant who earlier described the onset and progression of his symptoms, exemplifies one of these groups of cases. This group, characterised by ataxia and oculomotor disturbances, falls into the clinical grouping of spinocerebellar degenerations. Five individuals are currently affected by this disorder, four of them sharing one father. The other case is unrelated and currently lives at Numbulwar though he spent his school days and early working life on Groote Eylandt. The onset of symptoms is insidious and occurs in the fourth or fifth decade. Unsteadiness is the usual presenting complaint. Gait is ataxic and wide based, with arms outstretched seeking furniture or walls for support. When turning, staggering is prominent. Other signs of cerebellar dysfunction are present including incoordination, dysmetria, intention tremor and dysdiadochokinesis of both upper and lower limbs. Nystagmus, both at rest and on upward gaze, is present in the four more severely affected individuals, as is limitation of upward gaze. Convergent gaze is diminished in all cases.

The second syndrome is characterised by muscle wasting and weakness. Clinically it is a form of motor neurone disease, with a prenatal or at least early childhood onset. Weakness and wasting is predominantly distal and affects the lower limbs more than the upper. Muscle tone is generally low, although two of the older and more severely affected cases have increased extensor tone in the lower limbs. Deep tendon reflexes are brisk in most cases, especially in the lower limbs. Even in those cases with profound weakness and wasting, reflexes are generally surprisingly spared. Foot deformity (talipes equinovarus and/or pes planus) is universal and often noted at birth, strongly suggesting a prenatal onset. Spinal deformity (kyphosis or kyphoscoliosis) is also present in all but the most mildly affected. Striking laxity of the ligaments and small joint hyperextensibility is a prominent feature in most cases, demonstrated by spontaneous swan neck deformities of the fingers on extension and passive extension through > 100 degrees at the metacarpophalangeal joints. This suggestion of connective

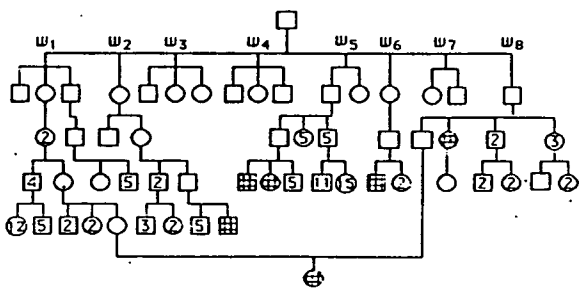
tissue disorder is supported by a curious soft, almost plasticene-like skin texture and mild skin hyperextensibility, but without evidence of abnormal scarring or easy bruising. Some of those affected with this syndrome are the children or grandchildren of individuals with spinocerebellar degeneration. The others with this syndrome are unrelated to anyone with spinocerebellar signs but can be grouped into a separate extended family pedigree. The inheritance shows a familial clustering but does not comply with a Mendelian pattern (Figure 1).

FIGURE 1.

A



B



A. Condensed pedigree of family 1.
B. Condensed pedigree of family 2.
Enclosed numerals represent numbers of offspring.
In B. "W" with subscript indicates wife number. None of the progeny of the offspring of wives 3, 4 or 7 are affected and so have been omitted.

Unaffected male Unaffected female
Case with amyotrophic syndrome
Case with ataxic syndrome
Unclassified neurological disorder

These two syndromes are linked by one pedigree which includes cases of both types, and an overflow of clinical manifestations between the two syndromes. One case, now deceased, presented a fusion of the features of both syndromes.

Finally I would like to discuss some recent blood manganese results. Earlier efforts at estimating manganese status of the Angurugu population had concentrated on analysis of scalp hair. This was because we hoped scalp hair may have provided a way of looking at more than just immediate manganese exposure. Serum manganese estimations are not only technically difficult, as evidenced by the wide range of normal values quoted in the literature (Halls and Fell 1981), but together with whole blood levels are also said to be of no value in diagnosis of manganese toxicity. As Dr. Florence has indicated, scalp hair manganese assays were increased amongst Angurugu inhabitants, but probably were still only representative of the rapidly turned over pool of manganese.

In November 1985, three brothers from Angurugu were transferred to Prince Henry Hospital, Sydney, for neurological investigations. Two were affected with the spinocerebellar disease and the other was a normal sibling. As a new assay for whole blood manganese had recently been developed at Prince of Wales Hospital, blood was collected from all three brothers. The results showed that the two affected cases had elevated whole blood manganese levels (640, 630nMol/L) while their unaffected brother had a normal level (390nMol/L). On receipt of these results blood was collected from a further five people affected by the motor neurone type syndrome and from four unaffected Angurugu Aborigines. The unaffected people were selected from a group who had had hair samples analysed and were two individuals with high hair manganese levels and two with normal to low levels (for Angurugu). Blood was also collected from a total of fourteen non Aboriginals, four resident at Angurugu and ten employees of Groote Eylandt Mining Company living at Alyangula. Including the results of the three brothers tested in Sydney a total of twenty six specimens have been analysed for blood manganese (Tables 1 and 2).

Analysis of these results shows that gross elevation of whole blood manganese levels is confined to Aboriginal residents of Angurugu who have neurological disease. Five of the seven cases with neurological disease tested show this elevation of whole blood manganese. None of the five unaffected Aborigines from Angurugu have high blood manganese. Although these numbers are too small to draw firm conclusions and the control group was not selected totally at random, there is a strong suggestion of an association between elevated blood manganese levels and the neurological disorder. This must be of concern, particularly as manganese is a recognised neurotoxin. While the neurological disorders found on Groote Eylandt do not correspond exactly with that classically described in manganese miners, the similarities are apparent. Yase (1972) found elevated manganese levels in spinal cord tissue taken from ALS patients from Guam and the Kii peninsular

in Japan, where high levels of this metal are present in soil and water. Recent studies have also found an increase in manganese levels in the spinal cords of patients dying with motor neurone disease (Miyata *et al* 1983 and Mitchell *et al* 1986).

TABLE 1.
Results of whole blood manganese analysis of Angurugu Aboriginals

Sample#	Blood manganese (nMol/L)	Sex	Status
1	640	male	spinocerebellar
2	630	male	spinocerebellar
3	710	female	motor neurone
4	660	female	motor neurone
5	170	female	motor neurone
6	285	female	motor neurone
7	770	male	motor neurone
8	465	female	unaffected
9	180	male	unaffected
10	305	female	unaffected
11	320	male	unaffected
12	390	male	unaffected

TABLE 2.
Results of whole blood manganese analysis of Non-Aboriginal residents of Groote Eylandt.

Sample#	Blood manganese (nMol/L)	Sex	Residence
1	160	female	Angurugu
2	175	female	Angurugu
3	105	female	Angurugu
4	90	male	Angurugu
5	405	male	Alyangula
6	110	male	Alyangula
7	180	male	Alyangula
8	165	male	Alyangula
9	230	male	Alyangula
10	195	female	Alyangula
11	125	female	Alyangula
12	115	male	Alyangula
13	140	female	Alyangula
14	115	male	Alyangula

It is unlikely that the elevated manganese levels found in neurologically affected cases is directly causal, as whole blood manganese probably reflects only very recent exposure. However it may be a marker of an abnormality in manganese metabolism which could predispose to manganese accumulation. If this is so, it should allow identification of those at risk. Another interesting observation is that even unaffected Aborigines living at Angurugu have higher blood manganese levels than Europeans living at either Angurugu or Alyangula. This suggests that some factor related to Aboriginality or an Aboriginal lifestyle predisposes to an accumulation of manganese in whole blood.

In summary I could demonstrate no evidence of increased congenital malformations or stillbirths occurring on Groote Eylandt when compared to another Aboriginal community of similar health status. There is however a strong suggestion of an association between elevated blood manganese levels and neurological disease. This must be cause for concern, particularly in view of the known neurotoxic potential of manganese. I am about to conduct a case control study in an attempt to clarify this apparent association.

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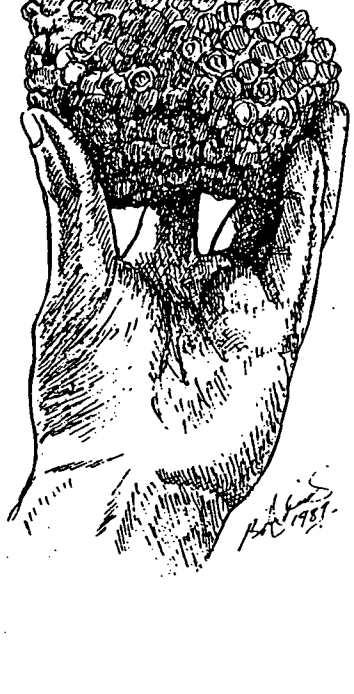

A nugget of manganese ore in the form of pisoliths, obtained in the village

WHAT ONE PATIENT TAUGHT ONE EPIDEMIOLOGIST

Professor John Cawte

What is epidemiology?

Epidemiology, according to my Webster's dictionary, is 1: a science that deals with the incidence, distribution and control of disease in a population (as of animals or plants); 2: the sum of the factors controlling the presence or absence of a disease or pathogen; 3: the ecology of a disease or pathogen.

For the mental health epidemiologist such as I, none of these definitions is really adequate. We can't study what are generally called diseases, though some of us give patients classifications that sound like diseases, such as mania, depression and schizophrenia. Most members of my profession consider this too narrow an outlook. When we study patients we look successively at a range of processes in the mental life, in the body, in personal relationships, and in the physical environment. We call our viewpoint holistic, rather than categorical. I teach students what I'd call "perignosis" rather than "diagnosis". That's what psychiatry is about.

Our work is complicated and time-consuming, and we are easily criticised by epidemiologists who want to ask more specific questions than psychiatrists usually ask, making the human problem more simple. It would be pleasant if it were! I learned psychiatric epidemiology in part from a famed Canadian teacher at Harvard in the 195[illegible] Alexander Leighton, who developed those historic studies of what he called "The Character of Danger" of a Nova Scotia community which he named *Stirling County*, and another he called by its correct name *Midtown Manhattan*. Some of his techniques can be found in my own book on this subject dealing with Australian tribal people, entitled *Cruel, Poor and Brutal Nations* (1972). This is the name that the Dutch explorer, Jan Carstens, gave to the folk of Mornington Island, south-east of Groote Eylandt. For today's purposes I only wish I had studied "The character of danger" at Groote Eylandt. We

should then be further ahead. I mention this work to show that I studied mental health epidemiology among tribal people, and that it is a different problem from what many more urban epidemiologists imagine. For a start, you have to be something of a linguist, an anthropologist, as well as an effective doctor, who wins their confidence through his relief of their sufferings. One must therefore smile, a little sadly, when experts who do not attempt these skills tell us from an office how to run our business.

We have worked on Groote Eylandt too briefly. For me it's mainly on vacations. The first thing I learned about this disease complex that affects them is that you can't classify it easily. It's not clearly spelled out nor defined in any of the books that I have read. I decided that I had to start with a single patient, offer a continuing relationship, earn his cooperation and then put together all the facts one could learn in those four domains in which he lived : his mind, his body, his society and his environment. Any of the four might help, none could be disregarded. Some facts fade and others grow bolder as time rolls by.

The single patient who has helped me most in defining this unusual problem has been kind enough to come here to this meeting today for you to meet him and hear his tale of illness. He has let me run some tests and trials to define his illness. I shall tell you about these tests, made in the hope that they will clarify. In doing this, he has shown courage, hope, persistence and cooperation - all stirling values in his make-up as a man. His English, and rapport with me is good, partly because he had training as a motor mechanic in Adelaide. He welcomes our team to Groote Eylandt not just for himself, but because of his concern for the future of his family and the other persons affected. There is a nobility about his suffering that deserves some recognition and esteem.

This man is 45 and has been increasingly affected for about 10 years. We shall not go into details of his symptoms here, as we have reported them several times in the literature. Neurologically, he is affected by an upper motor neurone disease - A.L.S., causing stiff movements, and by oculomotor disease causing poor vision and distance judgment, and by cerebellar disease causing poor balance and a wobbly gait on widely-spaced feet. He cannot walk backwards; he would fall. In addition to his spino-cerebellar disease, some judges would note signs of bulbar palsy. We have neurological test findings that confirm these obvious signs and symptoms but this is not the place to detail them.

He has been admitted to my hospital in Sydney, which locals call The Coast, on several occasions. Firstly he came with a group of other patients with similar conditions. Then he came with his wife and children, whom we lodged in the hospital's "motel" near the chapel, overlooking beautiful Little Bay and our own private beach surrounded by cliffs. Last November he came with two full brothers, an older one 55 and a younger one 35. The older is also affected but the younger is not. At weekends the four of us usually went driving - for example down the South Coast to see our old missionary friend, Mary Eves. So much for his inpatient status.

Let me indicate the various findings which he was the first patient to reveal. The same tests and studies might be offered to other patients. I cannot accept the criticism that Dr Kilburn and I have failed to carry out all these tests on everyone. Give us the time and the staff, and we will. When we have done all that, maybe we can conduct epidemiology in the sense our critics suggest.

HIGH BLOOD MANGANESE LEVELS

This patient was the first of the cohort to show a high level of manganese in the blood. Last November his level was found to be 640 nanomols (n mols). Mr Graham Hams today discusses the atomic absorption spectrometry he uses for trace elements in the Clinical Chemistry Department of the Prince of Wales Hospital at Randwick. At the same time, the level of brother "Senior" with a similar but milder neurological syndrome was found to be 630 namomols. I once freed "Senior" of a police charge of being drunk in a vehicle. I wrote a letter indicating that his staggering at that time was, in my opinion, probably due to this neurological disorder. The blood manganese level of young brother "Junior", who is unaffected, is much lower, at 320 nanamols.

But all these levels surprised us. The literature did not suggest they would be found. It has two half-lives, both fairly short, as Dr Florence tells us, and blood manganese only suggests recent exposure. Dr Kilburn conducted further blood tests in the vicinity, with similar findings in most of the neurologically affected patients, though normal

in others, including some Europeans. He will conduct more, at the Community's request, when he has time. Mr Graham Hams in Prince of Wales Chemistry is waiting for the samples.

Two neurologically affected subjects who live at Umbakumba do not show high levels of blood manganese. Apart from current non-exposure (the metal is not ambient there) I don't know how to explain it. Perhaps it is lack of exposure to manganese latterly? Perhaps it's a difference in susceptibility? - metabolic? - nutritional? - Family? - Other? We don't know. But look at my tables, 1 and 2.

Table 1

Manganese found in whole blood in 26 individuals at three townships of Groote Eylandt
(Note: initials have been coded to protect identity)

	Initials	Age	CNS Disease	Blood Mn. n mol/l
Aborigines in Angurugu	I.M.	Adult	Yes	630
	L.M.	Adult	Yes	640
	T.M.	Adult	No	390
	S.N.	Adult	Yes	710
	S.B.N.	Adult	Yes	660
	Q.S.	Infant	Yes	465
	H.X.	Adult	No	180
	T.N.	Adult	No	305
	U.M.	Adult	No	320
	W.M.	Child	Yes	770
Caucasians in Angurugu	M.L.	Adult	No	105
	D.L.	Adult	No	90
	K.X.	Adult	No	160
	M.E.	Adult	No	175
Aborigines in Umbakumba	E.C.	Adult	Yes	285
	N.C.	Adult	Yes	170
Caucasians in Alyangula	U.U.	Adult	No	405@
	B.X.	Adult	No	110
	C.K.	Adult	No	180
	K.O.	Adult	No	165
	H.B.	Adult	No	230
	E.O.	Adult	No	195
	M.C.	Adult	No	125
	N.U.	Adult	No	115
	L.X.	Adult	No	140
	E.T.	Adult	No	115

Note: Trace metal chemists have advised us of two reference ranges for this metal: 100-350 n mol/L, and 100-500 n mol/L.
@ This surprisingly high level, in an apparently well person, was replicated and found to be very similar on the second test.

Table 2

The time incidence of disorder of movement (limb weakness, cerebellar and eye movements and connective tissue disease) on Groote Eylandt, 1945 - 1985

Case No	Pedigree	Year of Birth	Sex	Onset	Weakness	Ataxia	Ocular Move-ments	Connective Tissue Disease
1	2	1982	F	Child	+++	-	-	++
2	2	1977	M	Child	+++	-	-	++
3	2	1975	M	Child	+	-	-	-
4	1	1972	F	Child	++	-	+	+++
5	1	1968	F	Child	+++/++	-	+/-	-
6	2	1962	F	Child	++/+	-	-	+++
7	1	1961	F	Child	+++	-	+	-
8	2	1960	M	Child	+	-	-	+++
9	1	1958	M	Adol	++	+	++	-
10	2	1956	F	Child	++/+	-	-	++
11	1	1945	F	Adol	++	-	-	-
12	1	1943	M	Adult	+	++	++	-
13	1	1940	M	Adult	+	+++	+++	-
14	1	1938	M	?Child	++	+	-	-
15	1	1939	F	Adult	+++	-	-	-
16	1	1935	F	Adult	+	++	+	-

CHELATION

Our friend here is also the first patient whom I tried to chelate. Many metals, of which lead is perhaps best known, can be removed from the body by administering substances which have an affinity for them, and are then excreted. I could have chosen penicillamine as chelating agent, but after a study of the literature I chose calcium versenate or Ca:EDTA.

Here is a summary from his hospital discharge summary of 3rd December, 1986:

> Other investigations were undertaken in conjunction with Dr Mark Florence of CSIRO. They included treatment with intravenous calcium EDTA in an attempt to boost manganese excretion in the urine. Results indicate that this indeed does promote manganese excretion and may have a place in prophylaxis of this condition for young Groote Eylandters.

Unfortunately for this hypothesis, Dr Florence later reported that the agent calcium EDTA itself may have been suspect of containing trace contents of manganese. Next time I shall get the agent tested by him beforehand, or use penicillamine. It should be noted, too, that Dr George Cotzias, the American investigator, found that chelation, even if it is valid, may offer little clinical comfort to established (chronic) sufferers.

CARBIDOPA ADMINISTRATION

He is also the only patient to have had Carbidopa, a form of L-Dopa. The substance was first given by this American, Dr George Cotzias in 1968 to affected manganese miners in Chile. It is still given to patients affected there by motor neurone disease, as it reduces their symptoms through its action on the neuro-hormonal profile. More recently (Guidice, 1986) found it to help rigidity and spasticity patients after head injury - voice and movement. They benefit from increased dopaminergic function and improve in consciousness. (Mary Ann Guidice is a Detroit neurologist). Dramatic advances were made in neuropsychiatry in the 1960s from improved knowledge of the neurotransmitters. In more recent times, increasing attention is given to the trace elements, especially manganese, in the production of catecholamines.

We did not then know that he had a high blood level of manganese, though we knew that he had a high hair level, through Dr Florence of CSIRO. I gave him *Sinemet* tablets containing Levodopa 250 mg and Carbidopa 25 mg. I made videotapes of his walking before, during, one week after, and two weeks after these treatments. I named the films "Red", "Blue" and "White" respectively, corresponding to the colour of his jackets. I convened a group of qualified neurological and psychological colleagues to appraise the performance on 10 parameters. These judges were not told of his condition, nor its treatment. "After treatment" scores showed great improvement. T tests showed $p<.001$. I shall now show you these films: see for yourself.

After *Sinemet* he walked faster and recovered his balance quicker after lurching.

After the first tape the patient was given a low dose of *Sinemet*, which was gradually increased over the next few weeks to a maximal dose of ¼ tabs q.i.d. The further two tapes were taken in the same setting, at weekly intervals. The patient felt improved, saying that his joints were less weak. He walked with less falling.

In my view there was also an improvement in his mental state. He was quicker in speech and thought. There was a lifting in mood, conversation and activity, with more attention and more smiling.

We discontinued Carbidopa treatment after he returned home, believing that he was again exposed to manganese. As well, this is not an easy treatment to supervise. Raising the dopamine by this means may deplete amino acids methionine and cystine, which should be supervised. Also, when this treatment is given for those affected by manganese, it is not usually given to those with structural damage, but only to more acute cases. This is the recommendation made by the WHO Health Criteria, anyway.

At least we studied how he responded to these two recommended approaches, chelation and L-Dopa. Manganese-exposed patients should be removed from the site of exposure. It might have seemed wise to most observers to suggest that he, and other neurologically affected patients, move to an unexposed site. Alas, for him it is HOME! We shall consider this problem later today.

Meanwhile, this single patient compelled us to study whatever was known about the role of manganese in health. For this we thank him. As suggested, possibly the best library source used to be IPCS - International Program on Chemical Safety, Environmental Health Criteria 17. MANGANESE, W.H.O. Geneva, 1981. Its contents might be indicated here, for those interested. It extends over 100 pages, including references. Other good sources will be cited in *References*.

ENVIRONMENTAL HEALTH CRITERIA FOR MANGANESE

WHO, Geneva, 1981

The Macassan beard copied from early visitors.

SOME CAUTIONS ON THE USE OF ETHNOGRAPHIC EVIDENCE IN MEDICAL RESEARCH

David Turner, Professor of Anthropology
University of Toronto

One of the current theories of the cause of the Groote Eylandt Syndrome is that it was triggered by a breakdown in the traditional Aboriginal marriage system. That is, it is a biological consequence of too close marriages or inbreeding. Indeed, in his article "Epic Accounts of a Mystery Illness" in the Australian and New Zealand Journal of Psychiatry (1984, Vol.18:179-87) Dr John Cawte reports that such an association was made by the Aboriginal people themselves:

> My informants maintain in effect that when the kinship and marriage system based on gerontocracy and polygamy was abandoned precipitously, in favour of the modern system of monogamy, the 'bird disease' emerged around the same time (p.185).

Marriages had, in fact, taken place which were "too close". It would be all too easy to see in this evidence of Aboriginal awareness of a relationship between inbreeding and illnesses like the Groote Eylandt Syndrome, and Cawte correctly cautions against doing so. The "too close" marriages in question are termed *warnigarangbidja* and refer to a situation in which the mother of the woman is in the same clan and generation as the father of the man (father and son are always in the same clan). Next to marrying within one's own clan and "side" (or grouping of clans of which there are four, further grouped into two), the closest marriage from the Aboriginal point of view is a *warnigaranbidja* one in which the man's father and the woman's mother have the same clan alliance histories, that is, are actual brother and sister. There is no evidence of any intra-clan or intri-"side" marriages within genealogical memory. As for the evidence of *warnigarangbidja* marriages, between about 1945 and 1969 the Aboriginal people allowed six such marriages to occur though none so close that the man's father and the woman's mother were actual brother and sister. However, as I report in my book *Tradition and Transformation* (Canberra: Australian Institute of Aboriginal Studies, 1974), "this decision was reversed and none of the ten marriages contracted since then (1969) falls within the prohibited category" (p.63).

That was in 1969 and it is now 1987. I have just completed a statistical analysis of the relationship system of the Groote Eylandt people, utilizing a computer simulation and based on data gathered in 1941, 1953, 1969 and 1986. It reveals that there has been no significant change in the social structure over this period. That is, clan affiliation and the rules of association between clans - including the rules of marriage - determine relationships and the terms by which people refer to one another to the same extent in 1986 as they did in the earlier periods. I have also recorded all marriages contracted since 1969 and the degree of "closeness" involved in them. Since I only completed this task last Sunday, I have not yet had time to fully analyse these data. However, it is evident that more *warnigarangbidja* marriages have occurred since 1969 but they constitute only a small percentage of the total marriages contracted.

At most, some 22 of 185 marriages, or 12% fall into the *warnigarangbidja* category. The majority seem to be located at Umbakumba and are concentrated in one clan there. There is no incidence of the Groote Eylandt Syndrome in this clan. In fact, of the 16 recorded cases of this illness, *none* of those afflicted had parents in a *warnigarangbidja* relationship.

While it is true that the "bird disease" emerged just after the first cohort of *warnigarangbidja* marriages took place, there is no basis for drawing a causal connection here. Groote Eylandt Aboriginal people also associate the appearance of the illness with the commencement of mining and it would be premature to draw any inferences between cause and effect here too. What Aboriginal people are doing is what any good scientist would do: formulate a number of testable hypotheses.

In his paper, Dr Cawte reported that some of his informants said that they believed the illness both "ran in families" *and* came from the environment.

What Aboriginal people mean by "runs in families" is not the same as what we mean or take them to mean. They mean they observe the fact that the disease is found more in some clans than others and is transmitted through the father all right, but not in the sense of biological inheritance. I am not at liberty to say more about this.

I would also like to caution on the use of ethnographic evidence relating to the presumed consequences of "too close marriages". For instance, "too close" marriages are believed to produce deformed offspring; a whole clan is said to have married within itself in the past and to have produced physically deformed children. But anthropology has shown that such stories are more imaginative constructs designed to convince members to obey the rules than statements of observed fact. To be taken as fact they must be statistically validated.

My statistics on *warnigaranbidja* marriage and the Groote Eylandt Syndrome show there is little basis for making an association between "closeness" and "deformity".

On the question of factual material relating to marriage practices and the Syndrome, it is worth noting that the two clans most affected by the disease - the Lalara and the Bara - never intermarry and have not done so within genealogical memory. Neither are indigenous to Groote, the Bara originating on Bickerton Island and the Lalara on Bickerton and before that on the adjacent mainland. Having taken up land in the north-western and central-western parts of Groote Eylandt respectively when they arrived here, however, they have been in the most prolonged contact with the most manganese afflicted parts of the island.

I hope these comments will prove of some use in further research into this illness and that a means of alleviating the symptoms and preventing its occurrence will soon be found.

It is well to remind the participants that as the medical debate over cause and effect in relation to the Groote Eylandt Syndrome goes on, and will go on, people are dying from this illness. Dr Cawte and his colleagues' researches have now given us some basis on which to process to stop this from happening.

Our friend Damiya, senior of the female health workers at Angurugu.

ANGURUGU SYNDROMES:

Should the Community consider relocation? If not, under which circumstances might it be safe to remain?

Interim suggestions from the Director of the Research Program:

Professor John Cawte

Workers in industries exposed to the substance manganese in high ambience are removed from further exposure right away, as soon as possible effects of toxicity are suspected.

Should the Angurugu Community Council consider this response? Much will depend on medical and chemical advice of the kind presented at this meeting. Some of our neurological sufferers are shown to have levels of blood manganese, and local topsoil and edible species are exceptionally infiltrated with high manganese levels.

Further research is being carried out to find if it will provide more guidance for the Community to decide. In my discussions with the Community over the years I have always emphasised possible toxic effects of living at a manganesed site. Relocation has not yet been closely considered, so far as I know, by any of the parties concerned - Community, Health Department, or Mining Community. All say in effect, "Do more research, Dr Cawte!"

It has, however, been suggested to me that two group of residents might wish to consider relocating from this site:

1. Those known to be ill, and showing manganese exposure by blood tests. Only a minority have suggested this. Angurugu is HOME to the affected people, who are chiefly in the Lalara and Bara clans. All I have spoken to want to stay - just as I stayed as a child at Port Pirie, S.A. where, at that time, the air was often infiltrated by lead from the local smelters. We all breathed it and hoped.

2. Those who might fear, after study of the facts, that there might be a problem about breeding children, bringing them up and generally living in this manganic environment

This second group, outside known patients and their families, would consist of islanders who have examined the health problems of living in an area of manganese exposure and consider that living at Angurugu may expose them to some risk. As indicated earlier, the most convenient and accessible account of the effects of exposure to manganese in the environment for them may be *I.P.C.S. International Program on Chemical Safety. Environmental Health Criteria 17. Manganese. World Health Organisation, Geneva, 1981.* Who is likely to read this?

Some scholars feel that W.H.O., in a 1981 summary, is already a little out of date. Knowledge and testing have been gathered since then on the environmental health problem; we have learned much more about the residents and environment of Angurugu in our own studies and we are hearing about it today.

A few people have suggested that they might choose to relocate for other reasons to set up a homeland community. They were interested in the challenge of selecting a good place to live with fresh water, safe soil, nearer to the sea for fishing, and then make good homes, roads, schools and services away from hazards such as habits of alcohol overuse and the sniffing of petrol. They said they can plan all this, with the experience of what can go wrong if it is unwisely planned.

I have usually replied when asked, that this sounds like very hard work. But many people benefit from hard work. There are usually enough good Aboriginal leaders able to inspire it in a challenge of this kind. It has to be the people's choice.

Talking at Angurugu, I have maintained since the first health conference at the Department of Health in Darwin in December 1983, that their Community home may not be safe for all living there even if for most people it is all right. In those days I lacked the knowledge of high manganese levels in the blood of some affected persons, and in the garden soil and edible species provided now by CSIRO.

In 1984, I thought I should suggest my concern to the Department of Aboriginal Affairs. I told them that the Community had asked my advice on their unusual illnesses, which have been called "Groote Eylandt" or "Angurugu" disorders. I reported that recent research literature was telling us that manganese exposure had toxic effects previously not recognised nor suspected. In brief, it is found to affect the nervous system, the development of the embryo, and the immune system, notably the defence against viral infection.

I said that I suspected that under these circumstances, some people, including unborn children, might be susceptible.

I did not want this view to be made prematurely public, because it would be challenged from all sides. The ensuing controversy could have profound implications for the Community and no doubt for many others, including the mining company, and the government, since the RAAF had caused the Community to relocate itself at this new site during the war.

I admitted then to the Department of Aboriginal Affairs that I could be quite wrong but I hoped, with its assistance, that a research grant might soon be forthcoming from the NH and MRC.

My natural concern expressed in this letter may have done some good, I think, because I did get some funding, and in the end our field researcher, Dr Charles Kilburn, began his work in the Community.

In today's Darwin gathering, in sharing what has been learned in more recent times, we have heard many minor items, and perhaps two major ones.

The first major item is the discovery of high levels of manganese in the blood of two neurologically affected brothers who were studied in my Sydney hospital last November. The chemist, Graham Hams, here today, talked about this test. He carried out similar identifications of high levels of blood manganese in several other neurologically affected patients whose bloods Dr Kilburn sent him early this year. We would like to have a much larger cover with these tests, but we did not think it fair to defer this meeting until we had them all.

The second major item is very high levels of manganese in the ambience at Angurugu, determined by Mark Florence, whose help we enlisted from CSIRO a few years ago. In addition, Mark found high levels of manganese in bush tucker that he collected locally, especially from the garden. He also determined another striking chemical factor, one which Dr John Hargrave and I already knew about - very low calcium. We shall have to decide if that is also relevant to health at Angurugu.

We have already told much of this tale to Mr Murabuda and his friends at Angurugu Council. I told Dr Keith Fleming, Professor John Mathews, Dr John Hargrave, Dr Gordon White, Dr Denis Stanbury and others. Finally, the Minister for Aboriginal Affairs, Mr Clyde Holding, invited me to Parliament House, Canberra to tell him what was going on. He suggested that I should report recent findings in the literature.

At the suggestion of Professor Fred Hollows, who works in my university, I chose to write a letter to the Editor of *The Lancet*. This is a fairly standard procedure in medical reports of new findings. My draft letter set going a train of responses, some helpful, a few indignant. I sent the draft to colleagues, like Dr Keith Fleming, Dr Robert Hart, Prof John Mathews and many others.

I made a personal trip, at a very busy clinical time, to Melbourne to see Dr Hart and his colleagues at BHP House, asking for ideas. They offered several responses, which I accepted, such as omitting from the letter to *The Lancet* the term "manganism" in favour of "high blood manganese", and omitting the name of the mining company.

Back in Sydney, I started to compose a telegram to the editor of *The Lancet* requesting these changes. Then I noticed galley proofs of my letter already on my desk. They had been delayed in reaching me in Sydney, I learned, by a U.K. mail strike lasting some weeks and still going on. So my first draft had been immediately accepted and published by *The Lancet*. Dr Mark Florence and I then wrote a second letter announcing the new finding of a high manganese level in the cores of soil at Angurugu and in the edible species. These two letters from my team are circulated with today's program for your awareness. Here they are:

THE LANCET, MAY 30, 1987

Letters to the Editor

MANGANISM IN A NEUROLOGICAL ETHNIC COMPLEX IN NORTHERN AUSTRALIA

SIR,—Accurate manganese analysis was developed, opportunely, at the Prince of Wales Hospital, Sydney, in October, 1986. The method is graphite furnace atomic-absorption spectrometry on a Varian P/L AA975 spectrometer equipped with a CTA95 furnace and sampler.

"Opportunely" because, in November, three brothers from a tribal Aboriginal family living at Angurugu, a township on Groote Eylandt, Northern Australia, were admitted for clinical study to Prince Henry Hospital, which is affiliated with the Prince of Wales Hospital. The brothers' ages are about 55, 45, and 35 years. The two elder ones have a neurological disease complex with upper motor neurone and cerebellar signs and oculomotor symptoms. The youngest is healthy, free of signs and symptoms. Although all three live in the same vicinity, the two elder brothers had worked, without masks, in a sampling mill of a company (GEMCO) established nearly two decades ago for open-cut mining of manganese ores, which exist mainly beneath the ground in the vicinity of this township. The youngest had not so worked.

The two affected brothers had whole blood manganese levels of 630 and 640 nmol·l. The adult reference range is still under review, but an early estimation is 100–350 nmol/l. A paediatric reference range is yet to be established. The affected brothers are part of a wider neurological cohort of at least 16 individuals in this tribally oriented Aboriginal community of about 1000 people. Most of these cases show clinically a range of dystonias, having gait, balance, and power defects. A relationship to manganese has always been considered possible.[1-4]

Observable in this local population are other unusual clinical conditions, including connective tissue disorders, congenital malformations and infant deaths, and psychiatric syndromes, usually expressing acute excitements. A resident medical officer is tackling the task, difficult in this population, of doing a preliminary survey of this related group of disease problems.

Some relationship has been suggested between these Groote Eylandt dystonias and the motor-neurone disease syndromes of the Western Pacific, which are associated with parkinsonism-dementia, described in Japan, Guam Island, and West Irian.[5] All these Pacific sites are located on about the same longitude (137°) and they share distinctive mineralogical features. However, no parkinsonism-dementia is obvious in the Groote Eylandt cohort, and there are other clinical differences.

In our search for causes we examined, and progressively eliminated from any strongly causal role: (*a*) genetic determinants associated with inbreeding, (*b*) deficiencies of calcium, iron, folic acid, and protein (all of which do exist here); and (*c*) toxic effects of local foodstuffs, such as an indigenous staple, the cycad palm nut, and introduced cassava crops. However, these syndromes occur in a region bearing manganese oxide ores such as pyrolusite and cryptomelane. These very black substances, used traditionally by native craftsmen and artists, are now industrially exhumed by open-cut mining operations, and manganese dioxide dust is often detectable in the air.

After the identification of raised blood manganese in the two brothers described above, over twenty tests were done on people living on the island, in its three townships. Very high concentrations, above 600 and 700 nmol/l, were found in the blood of four more patients affected neurologically. Unaffected Aboriginal subjects, and whites generally, show much lower blood manganese levels (150–200 nmol/l on average).

This Aboriginal community invited our research. It has now agreed to try to provide necropsy specimens for pathological study, especially of the nervous system, and we are attempting blood tests on the whole population to find out if there are further individuals vulnerable to what can now reasonably be termed the risk of manganism, environmentally induced.

Prince Henry and Prince of Wales Hospitals, University of New South Wales, Little Bay, NSW 2036, Australia

JOHN CAWTE
GRAHAM HAMS
CHARLES KILBURN

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THE LANCET, JUNE 27, 1987

ENVIRONMENTAL SOURCE OF MANGANESE ON GROOTE EYLANDT, NORTHERN AUSTRALIA

SIR,—Since our letter (May 30, p 1257), important findings have emerged which may shed a new light on the possible source of the manganese. Results now indicate remarkably high concentrations of manganese in surface soils and vegetables grown in the village concerned (Angurugu, on Groote Eylandt, Northern Territories, Australia). This suggests that local soil, dust, and plants may provide a more immediate source of this trace metal than the nearby mining operations. Examples will be cited here, in anticipation of more detailed publication later.

The manganese concentration of soil from Angurugu (the world average being 500 parts per million, ppm) was:

Source of soil	*Manganese (ppm)*
Orchard, open field	14 300
Orchard, under trees	33 400
Old vegetable garden	103 000
Banana plantation	41 900

The manganese concentration of locally grown foods (fresh vegetables worldwide having an average manganese concentration of 0·2–7·7 ppm) were:

Food sample	*Manganese (ppm)*
Banana, old garden	31·0
Native yam	720·0
Paspalum	240·0

It now appears possible that an immediate source of manganese could be the topsoil rather than the mining and crushing of underground lodes in this vicinity. Countering this presumption, however, is the fact that gardening and the close use of soils has declined over recent decades, since the first missionaries established the settlement. Nor do the native people eat much bush food; most of the food is bought from the village store.

Prince Henry Hospital,
Little Bay, NSW 2036, Australia — JOHN CAWTE

CSIRO, Lucas Heights, Sydney — MARK FLORENCE

SOME PRACTICAL SUGGESTIONS FOR THE COMMUNITY

Let us now review practical matters, assuming that the Angurugu people are wanting to stay, that the manganese is wanting to stay and that the mine is wanting to stay.

One cannot single out the mine for the problem. As Professor Kiloh and I long ago pointed out and Dr Joan Ridley read out today, several of the cases developed before the mine began operations. And, as Dr Florence pointed out today, there is an excess of manganese in cores of local topsoil, garden soil and in edible species.

A few suggestions do come to mind, two of which concern what I think of as some preventive value of another metal - iron. Critics may think my opening suggestion, an epidemiological one, is unforgivably "serendipitous". Here it is:

In 1970, I was invited by the East-West Centre in Honolulu to be a Fellow in Hawaii for a few months. That good break enabled me to publish two books, one on traditional Aboriginal healing and medicine called *Medicine in the Law*, and one on Aboriginal mental health epidemiology, called *Cruel, Poor and Brutal Nations*. Each subject is of unquestioned significance for students of Aboriginal health.

More importantly for today's purposes, living in Hawaii let me learn that a pineapple plantation seemed to have been affected by an excess of manganese in the soil, with this element appearing excessively in the fruit. I understood that this soil problem had been rectified by measured applications of a dressing containing ferrous sulphate. This was interesting then to me medically, but I did not take particular notice of it. Now, of course, I have written to a professional colleague in Honolulu asking for more information from the Hawaii Department of Agriculture, and maybe from the pineapple growers too.

I cannot be more specific about this until this information is assessed. It would be wonderful to see the soil problem in the Angurugu garden rectified in such a way and to watch the garden growing safe, fresh and varied food. I shall report on this to my colleagues as soon as I can.

The other issue with this "opponent" - iron - concerns its place in an individual's metabolism. We understand that iron deficiency, as occurs with the endemic hookworm anaemia, can promote bodily absorption of manganese. It is excellent that a local doctor is proposed by the Angurugu Council, supported by the N.T. Department of Health. Part of his or her program will be an all-out campaign against the hookworm and its anaemia. Another part should be the training of two Anindilyakwa mental health workers, a man and a woman, to deal with such matters as alcohol excess, petrol sniffing, and the all too common amotivational syndrome. I have been a leader of Aboriginal mental health para-professional training and I know what they can do. All these programs should happen, I hope, as outcomes of this research.

I respect the wishes of the Angurugu community to have all this done "in a quiet and friendly way". They do not want publicity. But they want general blood testing done to "pinpoint the sensitives", and we'll do it.

SOME PERSONAL MOTIVES

Some people here, not unsurprisingly, are unclear about my commitment to working in Arnhem Land continuing over so many years. A brief comment may explain and clarify. My motives are, or course, to do with Arnhem Land, Arnhem Landers and their wellbeing. I have had opportunities to study in some of the leading universities of the world, but I have to reflect that many of my personally significant educational and medical experiences have come from friends and informants in Arnhem Land, Australia.

In response to requests from up in that neck of the woods, I have undertaken several contracts which I hope to fulfil, while there's time. For example, visiting Elcho Island in my annual vacations for nearly two decades, I was affiliated with the Warramirri clan, former occupants of the English Company Islands and (maternal clan) the Wessel Islands. Warramirri were the great sailors of the Arafura Sea. Their complex religion saw their life as arising from the coral reefs, where the species develop in genetic leaps, recalling to me Darwin and Huxley's doctrines. But since they had to move to Galiwin'Ku, Elcho Island, they had not practised their religion openly. They asked me to record it, so that it would not die unknown. They provided the paintings and carvings of their Warramirri Heroes. I'm trying for funds to cover the art work of their book, which two university presses in Australia and USA have accepted on that provision.

Shortly after this, Kava misuse came to Elcho Island from the Pacific. I studied this condition clinically. My colleague Dr Alan Duffield is studying it pharmacologically under a NH&MRC grant at my university. We have made certain recommendations to the Federal Government about its currently misleading official excise as a "food substance".* My summons to Groote Eylandt inevitably interrupted my ongoing contracts with the Elcho Island people.

Academically, I'm indeed lucky to have some first-rate higher degree scholars in remote Australia. Dr Charles Kilburn needs no introduction today. Dr Ernest Hunter is studying the psychobiology of sudden death in the Kimberley, Western Australia. Perminder Sachdev is looking at the Maori migrant in Australia. Besides academics, I'm closely committed to Aboriginal health worker training, having originated the quarterly journal *The Aboriginal Health Worker* ten years ago, with help from the Department of Aboriginal Affairs. We employ an Aboriginal medical illustrator, Billy Reid, and a research assistant, presently Rose Ellis, for this Australia-wide quarterly, which is warmly greeted by its users. Naturally one concern is for Aboriginal mental health workers, whose training I helped to inaugurate in North Queensland. These commitments, of course, distract me from the disturbed Sydney folk whom I'm paid to treat, and teach student doctors to treat.

It may not surprise you that I've invited the B.H.P. Company to consider some personal support in the final part of my professional life, to enable me to tackle Arnhem Land and other Aboriginal contracts primarily. There are plenty of practitioners who don't want to work in the bush who can manage Sydney patients. I thought B.H.P. might like to consider this unusual request.

I'm by no means the only medical doctor in Australia with a "bush" - kind of research outlook. We are very gratified to see such a capable person as Dr Charles Kilburn, who spoke to us today, joining these ranks "in the bush".

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* The W.A. Government now classifies it as a "poison".

Now, it is time in today's conference to ask our expert panel to respond to questions and ideas from the audience, many of whom know a lot about this subject, more perhaps than they have ever said.

BIBLIOGRAPHY

The references to this work are numerous. Those who wish to study them will find a reasonably complete set in my two recent publications:

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AFTERWORDS TO THE CONFERENCE

After the Manganese and Metabolism Conference in Darwin, certain participants contacted us (John Cawte and Charles Kilburn) with considered comments. Most comments were too informal to quote here though they were appreciated. Most were supportive, though some were critical.

In this brief postscript we present several responses that are available and are likely to be of interest to readers. These include:

1. *The Press Release*, prepared after the Conference, in which the Secretary of Health, Dr Keith Fleming, managed to find a sufficient consensus among the audience to provide "a joint statement".

2. The newspaper account in The Northern Land Council's *Land Rights News*, from their reporter at the Conference.

3. The newspaper account in *The Sydney Morning Herald* of Friday, June 19, 1987, prepared by reporter Pilita Clark.

4. *Notes on Manganese at Groote Eylandt* sent to the chairman by the doyen of the Conference, W.C. Wentworth. These notes are quoted with his permission, not merely as a competent review of issues, but as the programmatic suggestions of the first Minister for Aboriginal Affairs. As chairman, I take the opportunity of presenting his notes with my personal tribute to their author.

5. *Farming High Manganese Soils in Hawaii.* Notes from correspondence to John Cawte.

6. *Discussion at the Conference.* We regret that we have no recording for a report of the comments made by participants at the Darwin conference. Many who were present at the colloquium presented their views, including Professor John Mathews of the Menzies School of Health Research in Casuarina, Darwin; Dr Robert Hart and Dr Michael Fett of BHP; Messrs Alan Wright and Sergio Fuenzalida of the Groote Eylandt Mining Co. Ltd, and others.

JOINT STATEMENT FROM MEETING, 11 June 1987,
at Health House, Darwin, Northern Territory

PRESS RELEASE

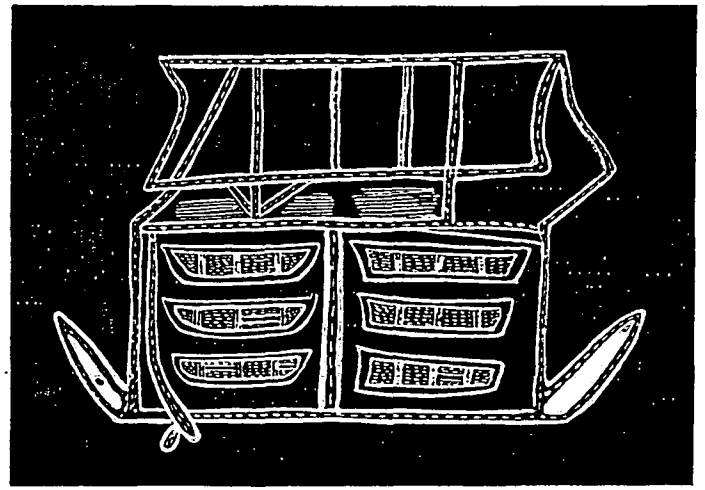
THE NORTHERN TERRITORY DEPARTMENT OF HEALTH AND COMMUNITY SERVICES HOSTED A MEETING TODAY IN DARWIN TO DISCUSS RESEARCH FINDINGS SO FAR INTO THE POSSIBLE EFFECTS OF MANGANESE ON THE HEALTH OF GROOTE EYLANDT ABORIGINES.

THE MEETING WAS THE THIRD HELD IN DARWIN SINCE THE PRESENT RESEARCH STUDIES, SUPPORTED BY THE NATIONAL HEALTH AND MEDICAL RESEARCH COUNCIL, GROOTE EYLANDT MINING COMPANY AND GROOTE EYLANDT ABORIGINAL TRUST BEGAN IN 1983 BY A TEAM LED BY PROFESSOR JOHN CAWTE.

PROFESSOR CAWTE INFORMED THE MEETING THAT HE HAD FULL DISCUSSIONS ON THE PROGRESS OF RESEARCH TO DATE WITH COMMUNITY LEADERS ON GROOOTE EYLANDT EARLIER THIS WEEK. THE PRESIDENT OF THE ANGURUGU GOVERNMENT COUNCIL WHO ATTENDED TODAY'S MEETING STRESSED THE NEED FOR FURTHER RESEARCH WHICH SHOULD BE DONE IN A QUIET AND FRIENDLY WAY.

THE MEETING EMPHASISED THAT THERE WAS A NEED FOR ALL INTERESTED PARTIES, PARTICULARLY THE COMMUNITY, THE GROOTE EYLANDT MINING COMPANY AND THE NORTHERN TERRITORY GOVERNMENT DEPARTMENT OF HEALTH AND COMMUNITY SERVICES TO CONTINUE TO SHARE INFORMATION AND JOINTLY FORMULATE A PROPERLY RESEARCHED AND AGREED PROTOCOL FOR FUTURE RESEARCH.

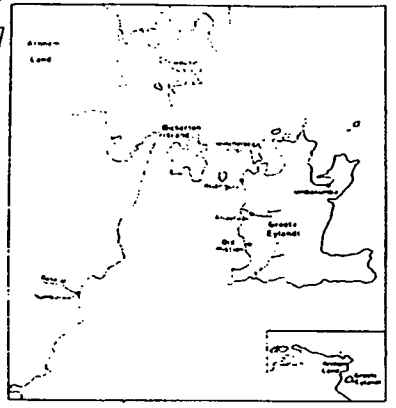
- ABOUT 2% OF ABORIGINAL RESIDENTS OF ANGURUGU, NORTHERN TERRITORY EXHIBIT UNUSUAL DISEASES OF THE CENTRAL NERVOUS SYSTEM.
- THE RESEARCH TEAM IS EXPLORING POTENTIAL CAUSAL FACTORS THAT INCLUDE EXPOSURE TO MANGANESE IN THIS ENVIRONMENT.
- FURTHER RESEARCH TO CLARIFY THESE ISSUES IS NEEDED, SUPPORTED BY THE COMMUNITY, GOVERNMENT AND THE GROOTE EYLANDT MINING COMPANY, INCLUDING TRACE METAL AND MEDICAL EXPERTS FROM OUTSIDE SOURCES, SUCH AS THE UNIVERSITY OF NEW SOUTH WALES, CSIRO, SYDNEY AND THE MENZIES SCHOOL OF HEALTH RESEARCH.
- MEANWHILE, SOME OF THE PRACTICAL MEASURES BEING CONSIDERED BY THE LOCAL COUNCIL TO REDUCE EXPOSURE INCLUDE SEALING OF ROADS AND RESTORING LOCAL HOUSING WITH LAWNS AND GOOD SAND.
- EMPHASIS SHOULD BE GIVEN TO EARLY DETECTION AND MEDICAL RELIEF OF THE NERVOUS SYSTEM DISEASES. TO ASSIST IN THIS, GROOTE EYLANDT LEADERS HAVE PROPOSED AN INITIATIVE THAT A RESIDENT DOCTOR TRAINED IN THIS FIELD IS PROBABLY NEEDED ON THE EYLANDT. THEY WILL INVESTIGATE PAYING HALF THE SALARY OF SUCH A DOCTOR TO MEET THE RESEARCH AND CLINICAL NEEDS. THIS PROPOSAL WOULD BE AGREED TO BY THE DEPARTMENT OF HEALTH AND COMMUNITY SERVICES. THE DOCTOR WOULD BE RESPONSIBLE TO THE COMMUNITY AND THE MENZIES SCHOOL OF HEALTH RESEARCH.
- DR CAWTE'S PRESENT RESEARCH TEAM WILL CONTINUE TO HELP IN THESE PROBLEMS.



The Malay Prau
by
Bakunda
From *Time Before Morning* by Louis Allen, 1975.
Crowell Co., New York.
The usual black background, made from ore,
features a great Macassan ship, anchored to the

'ANGURUGU SYNDROME'

Mystery illness strikes island



About two percent of the Aboriginal population of Angurugu community, which is surrounded by the BHP-owned Groote Eylandt Mining Company's manganese mine, has been affected by a mysterious neurological disorder.

The apparently small figure represents an epidemic by international medical standards.

A recent health survey has confirmed that at least 16 adults are seriously affected with the disorder, which attacks muscle control and is apparently untreatable.

Manganese may be the culprit. But its origin — either through the natural environment or because of massive disruption of the environment following the start of mining in 1967 — remains unclear.

Health authorities have known of the problem since 1933. A Sydney neuro-psychiatrist, Professor Cawte, who has been the prime mover in research programs into the disorder, went so far as to warn "an unmanned senior public official" in the strongest terms three years ago.

"Angurugu should be regarded as an unsafe environment and will remain so regarded unless proved otherwise," Professor Cawte said. No action has been taken on his warning.

DENIAL

Research to date has failed to establish any connection with mining. Although one of the causes attributed to the syndrome by Aboriginal people is the start of mining, BHP has been quick to deny the connection.

A BHP epidemiologist, Dr Robert Hart, said at a seminar held in Darwin this week that there was evidence of the syndrome from the days before mining began. No such evidence was presented to the seminar. The question of mining was not, in fact, raised at the seminar.

Another BHP official, Dr Michael Neff — who said he was speaking as a private citizen and not as an employee — questioned the very basis of five years academic and field research into the disorder. He claimed the results may have "fallen off the back of the truck" and had singled out manganese as the culprit in advance.

OVERLOADED

But one thing is clear — all the victims have excessive levels of manganese in their blood. The food they live from is loaded with manganese and fruit and vegetables grown in the soil show staggering manganese levels — in some cases 100 times higher than normal levels. Tap and river waters also contain high levels of manganese.

Participants in the Darwin seminar, including the Angurugu community, the Groote Eylandt Mining Company, the NT Health Department, the Department of Aboriginal Affairs and the research team, have agreed to continue research work. But the focus will shift from an independent approach to control by the NT Health Department.

Professor Cawte told the seminar that research was a long way from being concluded. He said the team had merely shown the environment was unsafe and isolated factors which may contribute. In a letter published in "The Lancet", he and other researchers said they had ruled out deficiencies in iron, calcium, folic acid and protein, all of which occur on Groote Eylandt. It has also eliminated the toxic effects of bush foods, including the cycad palm nut.

The possibility of a genetic cause, too, seems to have been ruled out by strong anthropological evidence which precludes the possibility of inbreeding. Anthropologist David Turner told the seminar that almost all affected people come from two clans — the Lalara and the Bara — which had never intermarried. Professor Turner, formerly a consultant to the NT Government, said none of the affected people were the offspring of close marriages.

NEW DISEASE

In a paper presented to the seminar, he also alluded to the difficulties of asking the Angurugu people whether the syndrome had ever shown up before — and particularly before the advent of mining. The people refer to a whole class of diseases as "Abrederegaraya", which covers leprosy as well as the "Angurugu Syndrome". Some informants, he wrote, have given a definite "No" when questioned about earlier outbreaks.

Papers written by Professor Cawte suggest that "Angurugu Syndrome" occurs elsewhere in the Western Pacific region. But a paediatrician who has carried out research on Groote Eylandt, Dr David Kilburn, was more cautious, saying it had "unique" features. Although the blood analysis showed heavy levels of manganese in the affected people this was no indicator of body storage. Yet other evidence points to the possibility of heavy concentrations of manganese in the brain — where it is highly toxic — and in other organs.

Laboratory tests on animals from Groote Eylandt — a melomys (mouse) and a dog — showed heavier than normal concentrations in the thymus, adrenal glands, spleen, cerebellum and brain membranes.

'NO TROUBLE'

Reaction from the Angurugu community has been muted. The President of the Community Council, Murubuda Wurrumarra, told the seminar it wanted no trouble with the Government or the Company. "We want to continue to be friendly together and carry on a normal life," Mr Wurrumarra said.

But so concerned about the syndrome is the community, in fact, that it has offered to pay half the salary of a doctor to continue research.

A seminar participant, Mr W C (Billy) Wentworth, unbelievingly praised this as an example of Aboriginal people's responsibility and initiative. Needless to say, the NT Health Department was quick to take up the offer. It will co-fund the doctor and use the Menzies School of Medical research to supervise the work along with the community.

But real action has been left to the community itself. The Community Council will take the responsibility of sealing roads to reduce dust loads and will replace garden soil with fresh sand and loam. Beyond the offer of funding, there appears to be no action contemplated by either the NT or Federal Governments.

QUESTIONS

The seminar has raised too many unanswered questions. While many people appear to accept the possibility of some genetic "trigger", or predisposition to the syndrome — which lies in the face of genealogical evidence — they balked at linking this with the natural environment, or with any disturbance to that environment.

Although the problem was first noticed by the Church Missionary Society as recently as late 1975, funding for proper research has been a long time coming. Had Professor Cawte not followed the problem personally, it may have gone unnoticed.

Will there be adequate funding and back-up for a full research program? Time will tell. Meanwhile, 16 people at Angurugu are in the grip of a baffling and incurable complaint.

Manganese: A short history

Manganese has long been recognised as an occupational health problem for miners and workers in processing plants.

An essential element in normal diet it can have toxic effects in overdose particularly when affected people are anaemic (low in iron), when they drink too much or if they have other dietary deficiencies.

In a mine or a processing plant symptoms can start to appear within months of heavy exposure, although they usually appear after about two years.

The first symptoms can be vague — headaches and lethargy — or there can be direct signs of impaired mental functioning.

Manganese actually catalyses the oxidation of dopamine, the neurotransmitting medium and creates toxic compounds in the brain including hydrogen peroxide, against which the brain has no defences.

PSYCHOSIS

In early clinical stages the symptoms of neurological damage predominate and can include speech and gait disturbances. The fully developed stage reveals manic or depressive psychosis and a similar condition to parkinsonism. If recognised early enough, it can be treated by removal from the exposure and dosages of calcium and vitamin B12. But the symptoms are usually confused with viral - type problems and may pass unrecognised.

Research into the problem began in the early 1950s with well-documented cases of Chilean miners suffering from manganese toxicity. There has been more recent occupational health research in the US, the Soviet Union and Europe.

It appears that the Angurugu studies may well be the first studies of an affected community near a manganese deposit (the Angurugu people are surrounded by an 80 sq.km. deposit of high-grade manganese).

Whatever the future may reveal, the implications are clear for occupational health measures within the Groote Eylandt mine. Workers should be asking themselves whether they are adequately shielded from exposure to heavy dust levels. And since the literature suggests that miners' wives may show a higher than average rate of miscarriages and stillbirths, perhaps the health of the non-Aboriginal community should be publicly monitored too.

The Sydney Morning Herald, Friday, June 19, 1987

Mysterious disease strikes Aborigines

By PILITA CLARK

An Aboriginal community living near BHP's manganese mine on the remote Northern Territory settlement of Groote Eylandt has been hit by a mysterious illness.

Health workers have reported that 16 of the 800 people in the Angurugu community have been seriously affected by the neurological disorder, which attacks muscle control and is very difficult to treat.

A Sydney neuro-psychiatrist, Professor John Cawte, who has been studying the disorder for nearly 10 years, said the incidence of such an unusual disorder is extremely high by international medical standards, even though only 2 per cent of the Angurugu population has been affected.

The findings of Professor Cawte and others were discussed at a seminar hosted by the Northern Territory Department of Health in Darwin last week.

The latest edition of the Northern Land Council's *Land Rights News*, which reported the seminar, says some Aboriginal people have claimed that one of the the causes of the "Angurugu syndrome" was the advent of manganese mining on the island in 1967.

But Professor Cawte is certain that cases of the disorder existed before BHP, the owner of the Groote Eylandt mining company, started mining in 1967. He was also grateful for the assistance that BHP had given for his research.

"Some people say that the mine has increased the level of exposure through dust in the air," he said, "but in my opinion, the more immediate source of exposure is from the topsoil and edible species.

All the victims have very high levels of manganese in their blood.

Fruit and vegetables grown on the island contain manganese levels up to 100 times higher than normal.

AN EDITORIAL REFLECTION ON W.C. WENTWORTH'S CONTRIBUTION

Readers will be struck by the immediacy with which Mr W.C.Wentworth, long since retired from public affairs and attending this conference from personal interest, grasped and summarised the cogent issues there presented. His response forms the basis of a suggested program of action, which he now offers for consideration. His action in doing this reflects the qualities of this first Minister for Aboriginal Affairs. The present writer has had other illustrations of this kind of intelligence and energy from him over past years.

It is characteristic of Mr Wentworth's resources to point out that his "Notes on Manganese at Groote Eylandt" were not the sole contents of the letter that he sent. He also enclosed, with no comment whatsoever, some photocopied extracts from C.D. Mountford's book on Ayer's Rock, to illustrate Aboriginal mythology about the infanticidal capability of the dingo, incidentally discussed at this time.

Hon. W.C. Wentworth

From the Darwin Meeting, 11 June 1987

NOTES ON MANGANESE AT GROOTE EYLANDT

1. It seems established that high levels of manganese in the body can cause both psychological and physical illness. Such high levels have been observed among both Aboriginals and Caucasians on Groote Eylandt.

   The soil on the south west of the island carries high manganese in many surface areas, which are generally underlain by the manganese ore which has been mined there by open-cut methods for a couple of decades.

2. Before the commencement of mining the Aboriginal inhabitants at Groote had the reputation of being psychologically disturbed, and this is some (not conclusive) evidence that "manganism" was prevalent there before mining.

   Available evidence suggests that present manganism does not come directly from mining operations.

3. Manganese may be taken up by the body in one of three ways :-

   (a) By absorption through the skin. This is believed to be of little consequence.

   (b) Through the lungs by reason of inhaled dust. This is believed to occur, although a great portion of inhaled dust ends up in the stomach rather than the lungs.

   (c) Through ingestion. This is believed to be the predominant method.

4. It is probable that, genetically, some individuals are more susceptible to manganism than others. It is not yet known whether any such susceptibility is commoner among Aboriginals than among Caucasians.

5. Instances of high manganese blood levels occur among inhabitants of the south-west area of the island, and are not confined to those who work in the mine or who are directly associated with it. The sample available is too small to allow firm statistical conclusions to be drawn from it.

6. Absorption of manganese in the body may be aggravated by :-

   (a) Iron deficiency, which is linked with the incidence of hookworm, which leads to anaemia.

   (b) Calcium deficiency, which may come from the phenomenally low level of calcium in Groote Eylandt soils, leading to some calcium deficiency in plants and animals entering into human dict. (It should, however, be recognised that Groote Eylandters are large consumers of imported foodstuffs which contain calcium).

7. The Aboriginal community at Groote is extremely concerned with the problem and has discussed paying half the salary of a doctor to be resident on the island. It is understood that official N.T. sources would be willing to provide the other half.

8. In these circumstances, the following programme could be considered.

   A. Appoint a director of the task force to go into the whole matter, using the services of the resident doctor who is to be appointed.

   B. Mount an intensive campaign against hookworm.

   C. Make available free pills with supplementary iron and calcium.

   D. Make available free blood and diagnostic tests for all Aboriginals who desire them.

   E. Shift the vegetable gardens to an area low in surface manganese, and enrich the soil with calcium.

   F. Make available alternative housing in manganese free areas for those at special risk (e.g., with high blood manganese, or families with pregnant women) who opt to leave the present settlement.

9. The campaign against hookworm could be developed intensively, not only for local effect, but as a pilot scheme for devising effective campaigns in all hookworm-infested areas. It could thus have a national impact.

   Similarly, study of manganism and ways to control it could produce results not just for Groote but for world manganese mining.

   These wider aspects, with their national and international implications, might be of interest to B.H.P.

FARMING HIGH MANGANESE SOILS IN HAWAII

John Cawte

Dr Mark Florence, from CSIRO at Lucas Heights, has told us about high levels of manganese in the soils and plant and animal life in the vicinity of Angurugu. Needless to say, Angurugu is not the only site in the world characterised by high soil and plant manganese. I learned of another during my visit to Hawaii in 1970 as a Fellow of the East West Center, which gave me the opportunity to write my books about Aboriginal healing and health, called *Medicine Is the Law* and *Cruel, Poor and Brutal Nations*, each published by The University of Hawaii Press.

Not being an agronomist or soil pathologist I will convey this subject for interested readers by quoting from some recent correspondence with Hawaiian experts.

Dr L. Ingamells, agronomist for the Dole Packaged Food Company in Honolulu, writes as follows:

> Soluble Mn levels in certain Hawaii soils are indeed high. Many years ago Mn toxicity was a subject of much interest in crops and soil science. Attached is a paper by Sherman & Fujimoto (1946) on work with vegetables in which Mn toxicity was effectively reduced by applications of lime or mulch.
>
> Work by H.Y. Young and his colleagues at the Pineapple Research Institute demonstrated that what was for many years considered Mn toxicity in pineapple could be corrected by foliar applications of Fe (P.R.I.Research Report No.84:45-56). Maxwell Johnson's earlier work with foliar Fe sprays in Hawaii helped establish the background for this, and the concept which emerged and was explained by Young was that there is an apparent optimum balance between Mn and Fe in the soil solution and in the plant. Thus, toxicity levels are difficult to establish for Mn because correction is always possible in the range found in Hawaii soils by the application of foliar Fe, at least as far as pineapple is concerned. Total Mn in pineapple tissue can range from 50 to 5000 ppm.

Dr Ingamells also sent an early publication which is classical. It is from *Soil Science Society of America* - Proceedings 1946, Vol.II, by G.Donald Sherman and Charles K. Fujimoto, pp.206-210. The title is - *The Effect of the Use of Lime, Soil Fumigants, and Mulch on the Solubility of Manganese in Hawaiian Soils.*

The opening part of this paper reads -

> The production of some vegetable crops in Hawaii has not been successful because of certain soil factors. One of the foremost of these limiting factors has been the high content of available manganese in the soil. Kelley was the first worker to report the abnormal manganese content of Hawaiian soils and its effect on plant growth. Later, Johnson discovered that the chlorosis which developed in pineapples grown on soils rich in manganese could be corrected by the application of a spray containing iron sulfate to the diseased plants. He concluded that the large amount of manganese in the soil oxidized the iron to the ferric state in which form it is unavailable to the pineapple plants. More recently, Fujimoto and Sherman have demonstrated that the quantity of available manganese present in lateritic soils depends on the soil temperature and the degree of hydration of the manganese oxides. They found that the available manganese increased with a rise in soil temperature, and if the manganese oxides are dehydrated, large quantities of soluble manganese will be released.
>
> Manganese toxicity to plant growth has been recognized in other soil areas. Funchess reported that certain nitrogenous fertilizers increased the soluble manganese content of the soil. Bortner corrected manganese toxicity in certain Kentucky soils with the application of lime and superphosphate. Snider has shown that the application of lime to the acid soils of Illinois materially reduced the manganese content of the crops. Recently, Fried and Peech have made a critical study to ascertain if acid soils required lime to correct other soil conditions. They concluded that one of the benefits of the application of lime to acid soils was the reduction of the soluble manganese.
>
> The application of lime to the Hawaiian soils having a high content of available manganese has produced a marked improvement in plant growth, however, this effect has not been as good as expected with those crops which are grown in rows. Another disadvantage found in the application of lime to Hawaiian soils has been the limited amount of lime which can be applied without the occurrence of overliming effects. Heavy applications of lime which are necessary to reduce the level of available manganese will depress the growth of plants very markedly. The maximum application of lime to Hawaiian soils without depression of plant growth is limited to two tons per acre. Thus, it is possible that the full benefit of the application of lime has not been obtained with crops commonly grown in rows due to the exposure of the soil to the sun which would produce a high soil temperature and which in turn would increase the soluble manganese in the soil.

This publication by Sherman and Fujimoto concludes as follows:

> From the results of investigations to determine the effect of applications of lime and soil fumigants and the use of mulches on the solubility of manganese in Hawaiian soils, the following conclusions may be drawn:
>
> 1. The application of lime to a soil decreased the exchangeable manganese in the soil. The application of 2 tons of hydrated lime to the acre decreased the exchangeable manganese about one-fifth of that found in the check soil.
>
> 2. The use of mulch which lowered the surface soil temperature and maintained a moist soil to the surface decreased the amount of exchangeable manganese present in the soil to about one-fifth of that present in the bare soil. This decrease was slightly less than that produced by the application of 2 tons of hydrated lime.
>
> 3. The application of 2 tons of lime to a soil with a mulch decreased the exchangeable manganese to about one-fourteenth of that present in bare soil which received no lime.
>
> 4. The application of soil fumigants, chloropierin and D'D' Mixture, did not decrease the exchangeable manganese in the soil. Both increased the exchangeable iron in the soil.
>
> 5. The yields of plants increased with a decrease in the exchangeable manganese content in the soil. The plant growth increased as the ratio of exchangeable manganese to exchangeable iron in the soil decreased.
>
> 6. The chemical analysis of plants revealed that the manganese content of the plants was closely related to the content of available manganese in the soil. The soil treatments which improved the plant growth produced plants with a lower content of manganese and a lower ratio of manganese to iron in the plant tissue.

As a final indication of the Hawaiian effort to combat this problem, I quote from a letter written to me from the College of Tropical Agriculture and Human Resources, at the University of Hawaii at Manoa. This letter is written by Y. Kanehiro, Emeritus Professor of Soil Science, and N.V. Hue, Assistant Professor of Soil Science. They write inter alia :

> After consultation with colleagues in our department, especially those familiar with growing pineapples in our high manganese soils, we have not come across any known case in Hawaii of manganese-caused illness in humans arising from consumption of food plants containing high levels of manganese. Upon further inquiries, we found out that Drs Nancy Johnson and Blubell Standal of the Department of Food Science and Human Nutrition are interested in this problem of Mn toxicity in humans and are presently conducting research on this subject. We recommend that for more information on their studies you communicate directly with Dr Johnson, Chairperson.

Concerning information in our department on manganese in our soils and plants, we do have some high manganese soils, and crops that grow in these soils suffer from excessive manganese Oxisols, total Mn_2 ranges from 1.79-5.22 per cent. Concretions found in these soils range from 27.9-30.8% MnO_2 (G.D. Sherman et al. *Soil Sc Science* 3(2):120-123. 1949). These soils are found in our drier regions that are subject to wet and dry seasons.

On soil management options on how to curtail uptake of Mn, past studies in our department have shown that mulching, trash application on soil surface, etc., i.e. practices that keep the soil relatively cool and moist, will decrease solubilization of soil Mn. Conversely, drying and heating will increase soluble Mn in these Oxisols. Liming will also decrease Mn solubility in these acidic soils.

As you probably heard during your tenure as a Fellow at the East-West Center, the common practice in pineapple fields is to apply iron sulfate to correct excess Mn uptake in the plant. This application of iron sulfate however is to provide an optimum Fe to Mn balanced uptake by the plant. Iron sulfate application does not substantially, if at all, decrease Mn concentration in the plant. On a related subject, the pineapple researchers have also discovered that the application of certain nematode-controlling fumigants will increase Mn availability.

In concluding this letter we would like to summarize and speculate that certain parts of a plant could accumulate Mn more than in other parts. There could also be certain plants, edible or otherwise, that accumulate extremely high amounts of Mn that we are not aware of.

We hope that the foregoing information/data prove helpful in your studies.

In reaction to this information, I suggest that it would be valuable if members of the Angurugu Council and the Church Missionary Society, together with a doctor, were to visit Hawaii to study this problem personally. It could make a difference to life at Angurugu if useful and safely supervised gardens were to be established in this way.

.....

A prayer for guidance of the Holy Spirit
in research and its application

God of wisdom and love,
Source of all good.
Send your Spirit to teach us your truth,
for the health and well-being of people,
and guide our actions
towards your way of wholeness.
We ask this thorugh Our Lord Jesus Christ,
your Son,
who lives and reigns with you and the Holy Spirit
One God for ever and ever.

AMEN

This is a benediction from The Right Rev. Clyde Wood, Bishop of the Northern Territory, and Mr Lance Tremlett of Angurugu, and the Church Missionary Society.

STOP PRESS: HIGH LEVELS OF BLOOD MANGANESE

This booklet is merely a state-of-the-art report for May 11, 1987. We also include some items omitted from the Darwin program. One concerns the local use of manganic ore for its black colour in painting and decoration. Another item concerns the management of highly manganic soils in Hawaii, to protect food plants. There, the Dole Pineapple Company and others use applications of cooling mulch between plants, with calcium and iron. These garden techniques seem successful. We recommend that an Angurugu team visit Hawaii to study them.

After the May Conference, one of us (Charles Kilburn) continued planned blood manganese estimations at Angurugu. High levels were found in residents other than those neurologically effected. Extra-ordinary levels of 800-900 units were found in a father and daughter, in a family not related to the two neurologically affected families. Blood manganese levels of this degree must give cause for concern, requiring close monitoring rather than medical laissez faire. In September, Charles Kilburn was obliged to return to Sydney and the NH & MRC appointment concluded.

A physician is urgently needed. The Chairman of the Community Council, Mr Murubuda, told the Darwin meeting that the Council would pay half of the salary required. Professor John Mathews of the Northern Territory School of Health Research, offered to supervise. The Church Missionary Society will maintain its longstanding care. We recommend a doctor who can offer general care, with a continuing study of "manganese and metabolism", including autopsy studies as occasion arises. Our thanks go to all who are concerned for this problem.

John Cawte,
Charles Kilburn.

THE ABORIGINAL HEALTH WORKER

POLICY

The Aboriginal Health Worker aims -

1) to assist Aboriginal health workers all over Australia to share ideas with one another;

2) to involve Aborigines and Islanders in all aspects of their health and adjustment, most especially in training and leadership roles.

This Journal assists health workers -

1) to diagnose and treat sick persons;

2) to explain sickness, its causes and its prevention, to the local community;

3) to tell the public, public servants, and politicians about Aboriginal health. Many of the decisions affecting Aboriginal health are not made by health workers.

Aboriginal health workers -

are all persons who help Aborigines rally from illness, or help them avoid being ill. Aboriginal health workers care for sick people in the homes, in the health centres, and in the hospitals. Most of their work is in the community.

Aboriginal health -

is the ability of Aborigines to rally from harmful effects in the environment, or the ability to prevent such effects occuring in the first place.

Requests to: The Hon.Editor, Dr John Cawte
Prince Henry Hospital
LITTLE BAY NSW 2036 Tel. (02) 694 5731 & 5660

A-90-16

Clinical Manganism and Exposure to Manganese in the Production and Processing of Ferromanganese Alloy

L. T. Smyth, M.D.; R. C. Ruhf; N. E. Whitman; and T. Dugan, M.D.

In 1963 the American Conference of Governmental Industrial Hygienists (ACGIH) changed the threshold limit value* (TLV) for manganese so that 5 milligrams of manganese per cubic meter of air (mg/cu m) represented a Ceiling Value.† In 1965, following the lead of the Threshold Limits Committee, the Pennsylvania Department of Health, under the Regulations Establishing Threshold Limits in Places of Employment adopted a Short Term Limit (STL) for manganese of 5 mg/cu m for 30 minutes.

As a consequence of those changes the medical and environmental quality control personnel of a large ferromanganese producer in Pennsylvania felt that a reappraisal of the environment and the health of employees working in ferromanganese production and processing facilities was indicated.

Manganism and Parkinsonism

The syndrome of manganism is that of Parkinson's disease and is clinically indistinguishable from it. A review of the literature elicits only about 400 cases of manganese intoxication since it was first reported over 100 years ago. Most of these cases occurred following exposure to manganese dioxide ore or to manganese dioxide fume produced by oxidizing processes such as cutting or burning.

Parkinsonism is a progressive neurological disease which results from destruction of the cells of the basal ganglia. Occasionally, it is seen as an acute illness following hemorrhage of the brain. Rarely, it is seen in association with brain tumor or syphilis. Arteriosclerotic, rather than primary degenerative changes, can occasionally be a cause of the shaking palsy of very advanced age. Until 1915, parkinsonism was mainly a disease of advanced age, rarely occurring before 40 and usually setting in between 50 and 60 years of age.

Poskanzer and Schwab (Massachusetts General Hospital, 1961) feel that most of the parkinsonism now seen is the result of the worldwide epidemic of encephalitis lethargica that lasted from 1915 to 1926. They expected that the number of cases would increase for some 40 years after the epidemic and then dwindle as the victims died from this or other causes. In 1961 the mean age of persons newly afflicted with parkinsonism was 60.6 compared with 34.7 in 1932. Poskanzer and Schwab subsequently examined 421 additional patients and found that none of them were born after 1931, the year the virus died out.

Cotzias[1] was the first to demonstrate a therapeutic response to high doses of levodopa. The rationale for its use had developed from studies showing that dopamine normally occurs in high concentration in the basal ganglia and substantia nigra, but at autopsy it was markedly depleted in those areas of the brains of persons having parkinsonism. Since dopamine does not cross the blood-brain barrier, its administration is ineffective. However, levodopa, the metabolic precursor of dopamine, does cross the blood barrier and presumably is converted into dopamine in the basal ganglia.

It is the opinion of some investigators (Penalver R, oral communication, and Whitlock et al[6]) that the parkinsonism syndrome produced by manganism is not progressive if the victim is promptly removed from exposure, and that the condition may improve following the use of chelating agents. Penalver has shown moving pictures demonstrating improvement in one case by simply removing the patient from further exposure, chelating drugs being not yet available.

Massive exposure to the fume or dust of manganese may rapidly produce symptoms and signs at any age in contrast to the slow and insidious course of parkinsonism due to other etiology.

The main portal of entry of manganese is the respiratory tract. The gastrointestinal tract plays little or no role and radioisotopic studies reveal that inorganic manganese salts are slowly and poorly absorbed by this route. The main route of excretion is in the bile, the liver being the preferred site of accumulation. Only small amounts of manganese are found in the urine, even following heavy exposure. Chelating agents, however, markedly increase the excretion by the kidneys. Manganese is an essential element for normal metabolism and with an average daily intake of 3 to 9 mg, the blood contains from 12 to 15 μg/100 ml and the urine

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somewhat less than 10 μg/liter.[2] Most of the intake is eventually accounted for in the feces. Maynard and Cotzias[3] demonstrated that manganese disappeared rapidly from the blood and was concentrated in the liver, kidneys, and brain.

Production and Processing Methods

From 1923 to the present, the production facility for ferromanganese at the operation under study has been the blast furnace. There have been changes, however, in the handling of the casted material. From 1923 to 1957, the ferroalloy was poured from the furnace into cast-cars (low-sided gondola railroad cars lined with refractive material). The casted material was removed from the cast-car and sized and sorted manually. In 1957, due to customer demand for smaller and more uniform sizes of the alloy, crushing and screening facilities were installed in the then existing building. In 1961, a new and larger building was erected to house crushing and screening equipment of much greater capacity. In December 1961, the molten ferromanganese was tapped from the blast furnace into conventional submarine ladles and transported to a pig-casting machine.

Nature of Exposure

Dust Exposure. — The mechanized crushing and screening operation resulted in the production of ferromanganese dust. Visual observation indicated that the overall dustiness associated with mechanical crushing and screening was greater than that associated with manual operations. Prior to 1960 dust was not generally recognized as being a hazard although Patty[2] stresses the mining, transporting, crushing, and sieving of the manganese ore as being the chief source of exposure and Voss[4] had reported one case of manganese intoxication in a man milling and grinding ferromanganese.

Dust sampling studies were therefore begun in the processing plant shortly after the commencement of crushing and screening operations in December 1960. At that time, the processing facilities were housed in a three-sided building measuring 335 ft x 106 ft (Fig 1). The south end of the building was completely open and there were large openings along both the east and west walls. On the west side close to the north wall, ferromanganese, which had been dug out of the cast-cars by Gradalls (an unloading machine with a claw-like attachment at the end of a telescopic boom), was loaded into boxes for charging into a jaw-type crusher. The crusher and screens were located at the north end of the building midway between the east and west sides. The finished product left the plant by truck through the large opening in the east wall and by rail from the open, south end.

Table 1. — Manganese-in-Air Dust Concentrations Before Ventilation — Old Preparation Plant

Type and Location of Sample	Number of Samples	Concentration (mg/cu m)*		
		High	Low	Average
Breathing Zone				
Crusher Operator and Helper	6	80.0	8.2	35.0
General Air				
Screening Station	6	52.0	9.0	27.0
Crusher Discharge	3	1750.0	405.0	1122.0
Screened Material	5	350.0	27.0	119.0

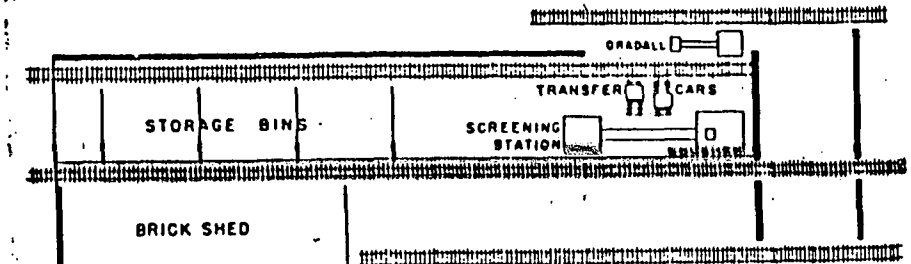
* Milligrams per cubic meter of air.

Because of the physical layout of the building and the working pattern of the employees, the midget impinger was used. (There were only two men, the Crusher Operator and Helper, both of whom remained fairly stationary on a platform atop the crusher.) Twenty samples, each of 15-minutes duration, were obtained over a two-day period in January 1958. The findings are listed in Table 1. Manganese-in-air concentrations averaged 1122 mg/cu m in the area immediately around the crusher discharge, which was the major source of dust. No employee was stationed in this area, though lesser concentrations (average 27 to 35 mg/cu m) were found in those areas in which employees were stationed, namely, on the platform atop the crusher and at the screening area. The time that employees remained in those areas of excessive manganese dust was not measured. Time-weight averages of manganese exposure, although obviously lower than the numbers cited, were also not determined.

At that time the TLV for manganese was 6 mg/cu m. Inasmuch as the dust measured concentrations were greatly in excess of that level, it was recommended that local exhaust ventilation be designed for all dust sources and installed as soon as possible. Until the ventilation system was operable, a respiratory protective program was made mandatory and initiated immediately.

In May 1959 an attempt was made to establish a procedure for monitoring the dust concentrations to which the employees in the Processing Plant were exposed. The felt filter pads were collected from the face pieces of the respirators after an eight-hour turn had been worked by the Crusher Operator and Helper. Filters from eight successive work shifts were obtained for each position. The filters were analyzed quantitatively for manganese by absorption that a man inspires approximately ten cubic

Fig 1. — Plan view of old manganese processing plant (building dimensions 335 ft by 106 ft).



meters[5] of air over an eight-hour work day, the exposures to manganese dust concentrations were calculated to be 47 mg/cu m for the Crusher Operator and 52 mg/cu m for the Helper. These findings were comparable to the 35 mg/cu m as determined previously by air sampling conducted in the breathing zone of the Crusher Operator and Helper. If one could with certainty know that the exposed employee was faithful in wearing his respirator, this procedure could be a useful method of monitoring the exposure. Because such assurance could not be given without constant supervision and because exhaust ventilation subsequently reduced the dust concentrations to acceptable limits, the procedure was abandoned.

Despite the installation of the crusher and rudimentary screening operation, some manual sizing with sledge hammers was still required. This work was performed near the open, south end of the building by four to six laborers. The laborers' total exposure to the dust created by their own work and by the crushing and screening equipment was determined by use of an electrostatic precipitator. Eighteen tests, each of approximately one-hour duration, were obtained over six different days in May 1959. The concentration of all 18 tests averaged 5 mg/cu m. Since the tests were conducted only during the time of processing and not during repair or lunch periods, the weighted-average concentrations would have been somewhat lower than 5 mg/cu m. Inasmuch as the measured concentrations were below the TLV of that time, the wearing of respirators was placed on a voluntary rather than a mandatory basis in that area of the building.

The installation of the exhaust ventilation system was completed in February 1960. During March 1960, in order to evaluate the efficiency of the new system, air samples were collected with a midget impinger and an electrostatic precipitator on the platform atop the crusher and in other work areas around the crusher and screens. The manganese dust concentrations averaged 0.7 mg/cu m atop the crusher and 0.6 mg/cu m in the adjacent work areas; the highest concentration was only 1.84 mg/cu m. This was a dramatic improvement over the excessively high levels measured prior to the installation of the exhaust system.

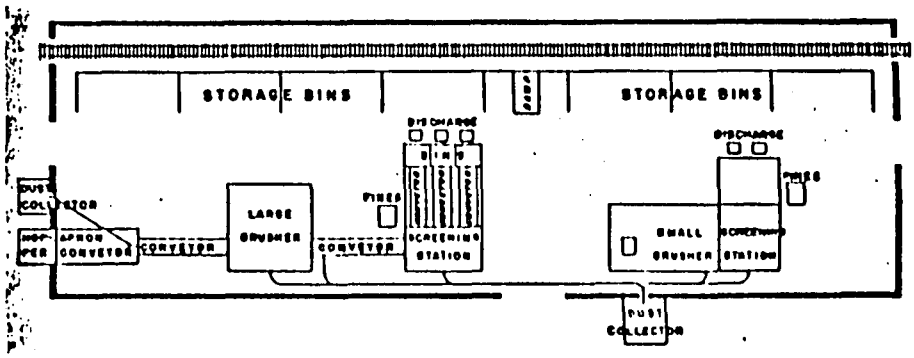


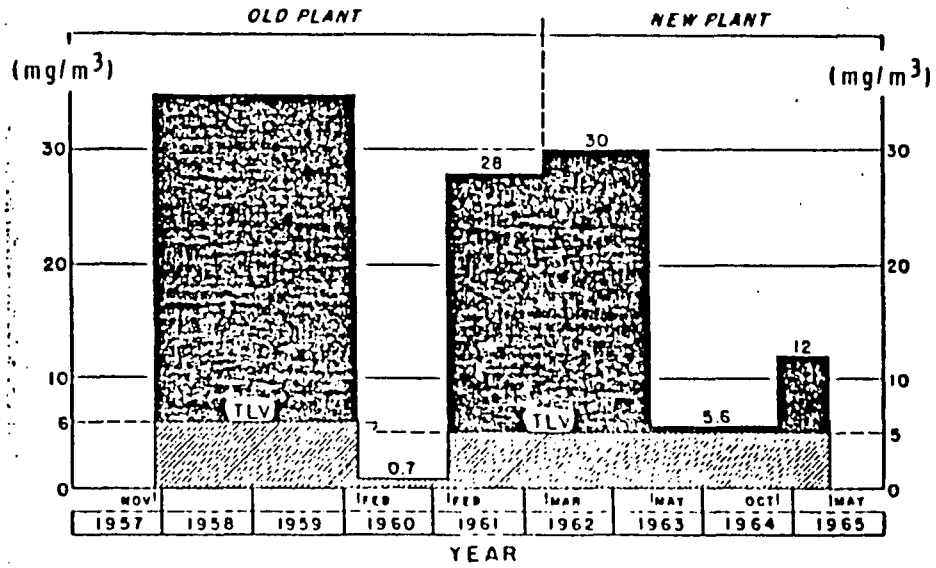
Fig 2. — Plan view of new manganese processing plant (building dimensions 400 ft by 128 ft).

Because of the extreme abrasiveness of the dust, however, the ductwork in the ventilation system soon began to erode, particularly in the elbows, where holes began to appear. In addition, because of the bulkiness of the large and heavy loading boxes which required frequent moving, inadvertent damage to the hoods ensued. Both these factors contributed to a gradual reduction of the air volume needed to satisfactorily transport the contaminant from the work areas. Further atmospheric testing to determine exposure to manganese dust was conducted during January and February of 1961. Ten tests in the breathing zone of the Crusher Operator and the Bottom Man (employee working primarily in the area around the screening equipment, who was responsible for seeing that sized material from screening operations was properly loaded and removed for shipping) were obtained with a midget impinger over four different days. The average dust concentration immediately following installment of the ventilating system was 3.2 mg/cu m for the Crusher Operator and Helper (about a fivefold increase over that of the 1960 study), and 53 mg/cu m for the Bottom Man. Because of these relatively high dust concentrations, management was urged to make every effort to maintain the ductwork and hoods and require the wearing of respiratory protective devices when excessive dust concentrations were encountered.

Because customers demanded a wider range of small sizes of the alloy as well as varied manganese composition (range 74% to 82%), it was necessary to purchase another crusher, smaller in size than the original, but of the same type. It was also decided to house the crushing and screening equipment in a new and larger processing building (Fig 2). By March 1962 the changeover was completed. At the same time the old "large" crusher and screens were supplemented with the new "small" crusher and its auxiliary equipment.

In the new processing building an attempt was made to use water sprays as a

Fig 3. — Summary of average ferromanganese dust concentrations.



dust suppressant at material transfer points in lieu of hoods and exhaust ventilation. It was apparent from the start that sprays, while accounting for some reduction, were not lowering the dust concentrations to satisfactory levels. To confirm these observations, general air samples were obtained with an electrostatic precipitator during June and August 1962. Concentrations during this study ranged between 12 and 83 mg/cu m and averaged 30 mg/cu m. Based on these tests it was recommended that water spraying be discontinued and an exhaust ventilation system be installed. In May 1963 the exhaust ventilation system was completed for both the large and small crushers as well as their respective screening equipment.

Sampling of the air-borne contaminant by midget impingers to determine the effectiveness of the new ventilation system was completed by October 1964. Twenty-five general air samples, each of 10- to 12-minutes duration, were taken over the various working locations during the survey period.

On five of the nine test dates, the average daily concentration exceeded the TLV for manganese; of the 25 samples, nine exceeded 5 mg/cu m. However the average concentration (5.6 mg/cu m) of all the samples was just slightly above the TLV.

Fig 3 shows that between November 1959 and May 1965 average ferromanganese dust concentrations in the processing plant were in excess of the TLV for much of the time.

The processing plant operation requires periods of down-time during the course of a work day because of the necessity to change screens for the varied sizes produced and for crusher malfunction. The average concentrations expressed in Fig 3 reflect both periods of down-time as well as periods of peak production. In spite of that, it is apparent that for appreciable periods of time over the 7 1/2-year period (1957 to 1965) employees were exposed to higher than desirable levels of manganese and during the periods when local exhaust ventilation was not operative, average concentrations were three to six times the TLV.

Fume Exposure. — At this operation, ferromanganese is produced in a blast furnace. Ferromanganese fume is emitted during the 20 to 30 minutes of the cast as a dense, orange plume which arises from the trough running from the blast furnace to the ladle and slag pots and spreads rapidly over the cast house floor. Because of the natural movement of air across the cast house floor, the plume is rapidly dissipated following the conclusion of the cast.

The First Helper experiences the highest exposure due to the fact that his work requires him to maintain a position relatively close to the trough during the entire cast. Other employees are able to remain in the Blowers Shanty (enclosed control room) or at the furthest upwind portion of the cast house away from the most dense portion of the plume.

The exposure at the pig-casting machine is also to ferromanganese fume arising from the runner leading from the ladle to the pig moulds. The exposure lasts for about 1 1/2 to 2 hours per pouring operation (5 times per 24 hour period).

The Pourer's exposure is greater than that of the Tilter because of his working position in relationship to the runners conveying the molten metal. His work requires him to maintain the runner (clearing slag, etc) in close proximity to the source of the fume, whereas, the Tilter is in an enclosed pulpit and at some distance from the plume.

In early 1964 a significant event which occurred in a plant in central Pennsylvania was brought to our attention.[6] Two men employed to cut and trim manganese steel castings with air-arc burners in a small, unventilated enclosure were admitted to a Harrisburg, Pa, hospital with symptoms and signs of central nervous system impairment manifested by progressive weakness, unsteadiness of gait, loss of co-ordinated movements and increasingly severe hoarseness of the voice. There was marked loss of strength in all extremities, abnormal reflex changes, intention tremor and a sense of euphoric, carefree attitude not previously characteristic of the personality of the employees. An inexpressive facial masking was present as well.

Following EDTA† treatment, there was an immediate high excretion of urinary manganese (as much as 1,000 µg/liter in one patient) and, with the passage of time, an improvement in the clinical appearance of the employees. It was concluded by the authors that the TLV for manganese-in-air concentrations provided little or no factor of safety, thus confirming the opinion expressed by the ACGIH Threshold Limits Committee when a ceiling value was established. In effect, this event indicated to the investigators that serious manganese intoxication might occur when weighted manganese-in-air concentrations were below the TLV as then defined: 5 mg/cu m (ceiling value).

Our attention was now directed to production of ferromanganese at the operation being studied because of the recognized manganese fume exposure which we believed might be similar to that of the reported cases in the Harrisburg area. In February 1966 it was decided to perform an epidemiological study of the entire problem.

Environmental Phase

Method of Study. — Fifteen positions, as indicated by previous environmental sampling and observation to have the highest exposures, were to be studied; nine at the production (fume) area and six at the processing (dust) area. Since the Pennsylvania STL for manganese is based on a 30-minute period, all air samples throughout the study were collected for this length of time. All air samples were taken in the worker's breathing zone and sampling was done in all four seasons of the year.

Fume. — For the fume exposures the electrostatic precipitator was used as the basic sampling instrument. That instrument, however, requires the investigator to hold the sampler in the vicinity of the worker's breathing zone. Since some job positions, such as the First Helper on the Cast-House floor, were too hazardous to permit that procedure, the electrostatic precipitator was supplemented with the millipore filter and monitaire pump which could be mounted on the employees.

Before the study was begun, simultaneous sampling with the electrostatic precipitator and millipore filters was performed and it was determined that results obtained from the two methods were comparable.

The survey of the nine job positions at the production facilities consisted of collecting air samples during the casting of the furnace and during the pigging operations. Additional samples were obtained before and after casting and pigging to determine concentrations to which the employees were exposed

during the intervals between the times of fume production.

Dust. — For the dust exposures, sampling was done with the midget impinger, the collecting flask being suspended from the worker's shirt. The monitaire pump was the vacuum source. Early in the study it was determined that the midget impinger samples were being contaminated. Millipore filters, which were difficult to inadvertently contaminate, were substituted for impinger flasks. Testing showed that the results obtained by the two sampling techniques were comparable and the millipore filter sampling method was used for the duration of the study.

In the Preparation Plant, where the ferromanganese is processed almost continuously, samples were collected over the entire three workshifts for the six positions being studied.

Results

Fume. — Table 2 summarizes the results of the breathing zone samples by position at the Blast Furnace and Pig Caster. The number of samples and the range as well as the weighted-average concentrations for each job position are shown. In addition, the number and percent of samples exceeding the short-term limit are listed.

At the Cast-House none of the job position exposures exceeded the TLV of 5 mg/cu m. The highest weighted-average concentration (3.6 mg/cu m) was found for the First Helper and the lowest (0.12 mg/cu m) for the Cinderman. On the other hand, the short-term limit was exceeded on numerous occasions at six of the seven positions.

At the Pigging Machine, the Pourer's exposure (13.3 mg/cu m) was in excess of the TLV, whereas, that of the Tilter was slightly below (4.4 mg/cu m). However, 93% of the samples for the Pourer and 75% of the samples for the Tilter exceeded the STL.

Fig 4 shows the particle size distribution of the air-borne fume. One hundred percent of the fume is composed essentially of manganese oxide, but mainly Mn_3O_4, and is less than 2μ in size, all of which is respirable.

Dust. — At the Crushing and Screening Plant, as is seen in Table 3, the TLV was exceeded at three of the six positions studied. Those included the Screen Plant Helper (12.9 mg/cu m), Screen Plant Operator (6.3 mg/cu m) and Fork-Lift Operator (5.2 mg/cu m). As was the case in the Production Facility many of the samples were in excess of the STL.

Table 2. — Manganese Fume-in-Air Concentrations by Position

Position	Number of Samples	Samples Exceeding Short Term Limit (STL)		Concentration (mg/cu m)		
		Number	% of Total	Low	High	Weighted-Average
Blast Furnace Casthouse						
Keeper	16	5	31.00	0.04	39.6	1.06
Blower	16	5	31.00	0.04	39.6	1.34
Hot Blastman	13	1	0.83	0.02	5.9	0.33
Turn Repair Pipework	6	4	67.00	0.05	12.7	1.28
Second Helper	9	2	22.00	0.34	9.4	0.51
First Helper	10	7	70.00	2.20	171.0	3.60
Cinderman	8	0	0.00	0.02	1.9	0.12
Pig Casting Machine						
Tilter	24	18	75.00	3.02	43.9	4.40
Pourer	14	13	93.00	3.20	206.0	13.30

Particle size distribution of the air-borne dust was determined and is plotted in Fig 5. Ninety-five percent of the dust is less than 5 μ in size, and is of respirable size.

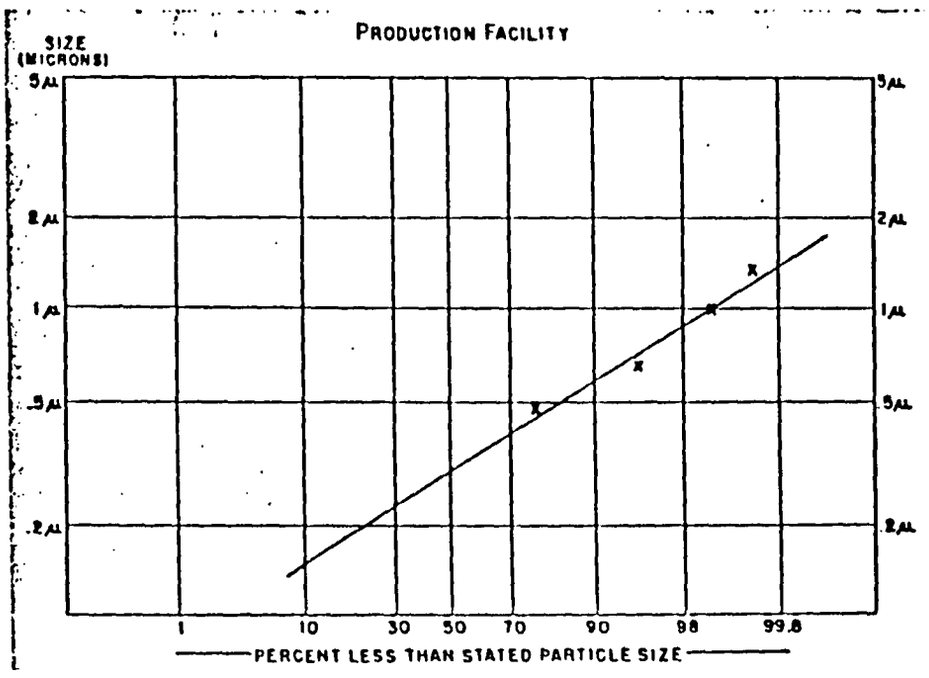
The dust was analyzed for its chemical composition by x-ray diffraction and infra-red methods. Results showed that the metallic content of the dust was mainly ferromanganese (FeMn) with small amounts of manganosite (MnO), Hausmannite (Mn_3O_4) and iron oxide (Fe_2O_3).

Clinical Phase

Method of Study. — It was decided that a study of 71 employees, exposed daily for eight-hour shifts in three areas involving 15 positions, would render the greatest information. A second group of 71 male employees was selected for identical study. These men, chosen from the plant generally and never having been directly exposed to manganese, were matched for age, length of plant service, and ethnic background.

The routine procedures on all persons studied included a history, physical examination, and certain laboratory examinations. All employees received an examination by a neurologist. Blood slides for stipple cell counts were examined by a pathologist. Urine and blood manganese assays were performed using a method especially developed for this purpose.[7] The neurological examination, stipple counts, and blood and urine assays were

Fig 4. — Particle size distribution of airborne fume (production facility).



performed as blind studies to insure objectivity. Additional laboratory studies included chest x-ray, red blood cell count, white blood cell count with differential, hematocrit reading, blood sugar, sedimentation rate, urine analysis, and electrocardiogram.

Results. — Examination of the 142 employees elicited five cases with symptoms and signs of central nervous system impairment highly suggestive of manganism. All five were from the exposed group and all but one occurred in positions of highest manganese exposure. Three were exposed to manganese fume and two were exposed to dust.

The salient features of each case are listed below.

Case 1. Age 47. Twenty-three years intermittent exposure to ferromanganese dust as an Unloader, Screen Plant Operator, and Helper. When examined was found to have had history of parkinsonism for five years. Clinically he exhibited marked masking of the facies, loss of blinking reflex, absence of associated movements of the left arm when walking, tremor of left arm and head, and cogwheel rigidity of left arm and leg. There was micrographia.

Case 2. Age 48. Twenty-three years intermittent exposure to ferromanganese dust as an Unloader, Screen Plant Operator, and Helper. When examined he had no complaints but on neurological examination he exhibited complete loss of associated arm movements bilaterally.

Case 3. Age 52. Eight-years exposure to manganese oxide fumes, three years as a Laborer in the general blast furnace area, and five years as an Iron Pourer at the Pig Casting Machine. Clinically he had no complaints, but on neurological examination exhibited complete loss of associated arm movements bilaterally.

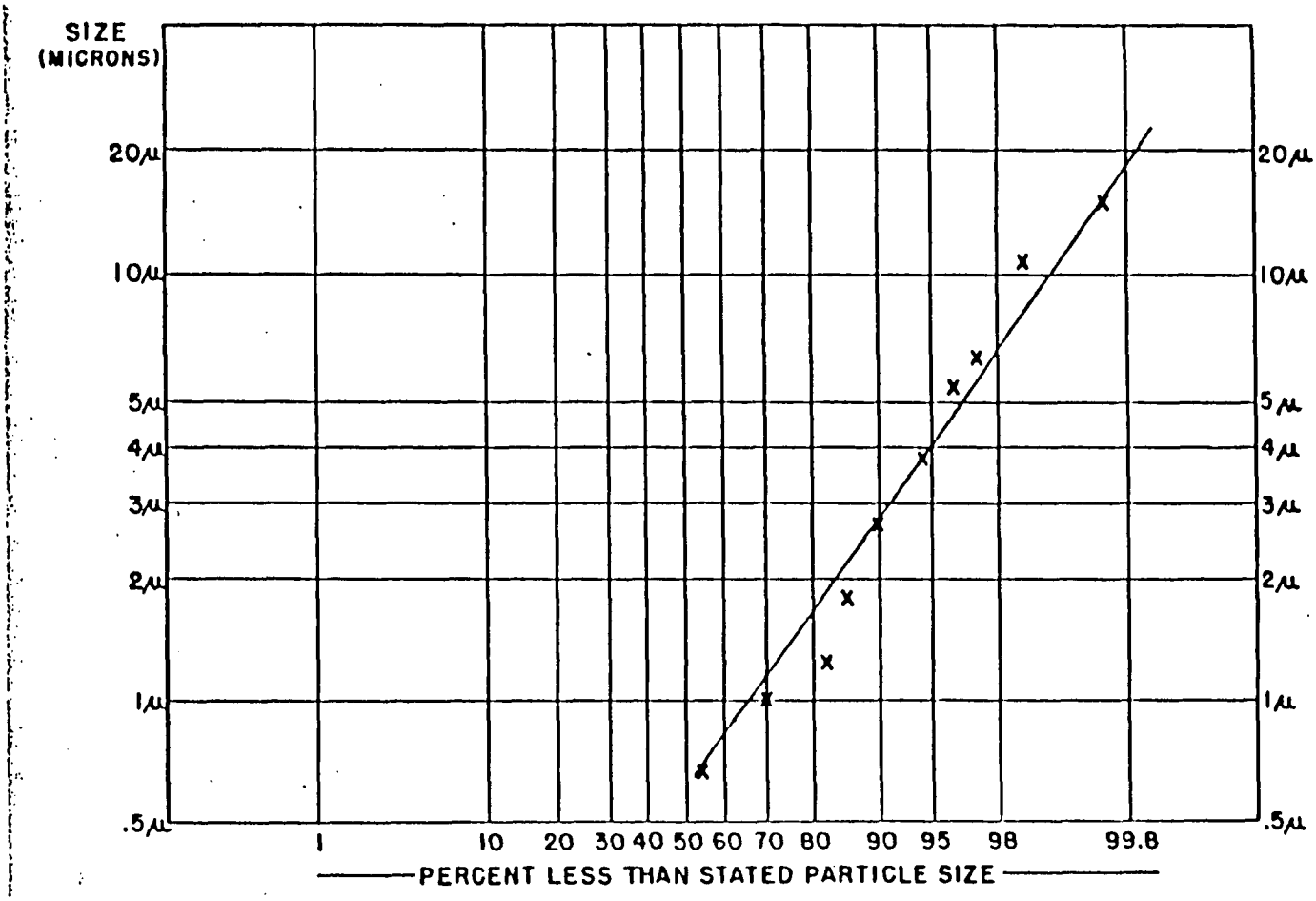
Case 4. Age 49. Twenty-six years intermittent exposure to manganese oxide fumes as a Laborer and Iron Pourer at the Ferromanganese Pig Casting Machine. Clinically exhibited marked masking of the facies, diminished blinking of the eyelids, absence of associated arm movements, muscle rigidity in right arm and both legs. Micrographia was present.

Case 5. Age 49. Ten and one-half years exposure to manganese oxide fumes as a Hot Blastman at the Ferromanganese Blast Furnace. Clinically exhibited micrographia, loss of associated arm movements on the right, and static tremor of the right hand. There was facial masking, reduced blinking reflex, and some cogwheel rigidity in the right arm and leg.

None of the five employees admitted to early complaints of languor, lassitude, or apathy. All five were actively working and one (Case 2) lived on a farm and was productively working it in his spare time. There was no noticeable difficulty in walking or speech impairment. There was no history of muscle cramps, headache, loss of sleep, or excessive sweating as have been reported. Case 5 exhibited excessive salivation and a tendency to drool. No pathologic reflexes were present. None of the employees remembered having been told by family members that they have been influenza victims in infancy or childhood. Neither had any suffered from pneumonia since being employed. (Pneumonitis has been reported as a manifestation of manganism.)

In reviewing the sick absence records for the five employees, it was noted that Case 2 had been ill from January 24,

Fig 5. — Particle size distribution of airborne dust (manganese shed).



1952, to July 13, 1952 (182 days), with a diagnosis of "Psychosis" which we believe may have been representative of a transient personality change. When questioned about the episode, the employee stated he "trembled" when he tried to perform fine mechanical tasks such as threading a nut on a bolt and he would "break out into a sweat." However, the nature of the incident is not clear and its significance unknown. The personality of the employee at the time of examination was "normal" in every respect. Nevertheless, the episode did occur during a period of exposure to ferromanganese dust.

The five employees were hospitalized for further study under the care of an internist. Results of skull films, electroencephalograms, spinal taps, and blood serology were negative for all. Serum iron and serum iron binding capacities were normal. Red blood cell counts, hemoglobin values, white blood cell and differential counts were within normal ranges. Case 2 revealed fine, delicate stippling in a very occasional red blood cell. Case 3 revealed a hypertension with left ventricular hypertrophy and a history of familial hypertension.

Upon hospital admission, collection of 24-hour urine specimens were begun and continued for ten days in Cases 1, 3, and 4; four days in Case 2; and three days in Case 5. The average urine manganese concentrations for the five cases are shown in Fig 6. Except for Case 5, the average manganese concentrations were below 10 µg/liter.

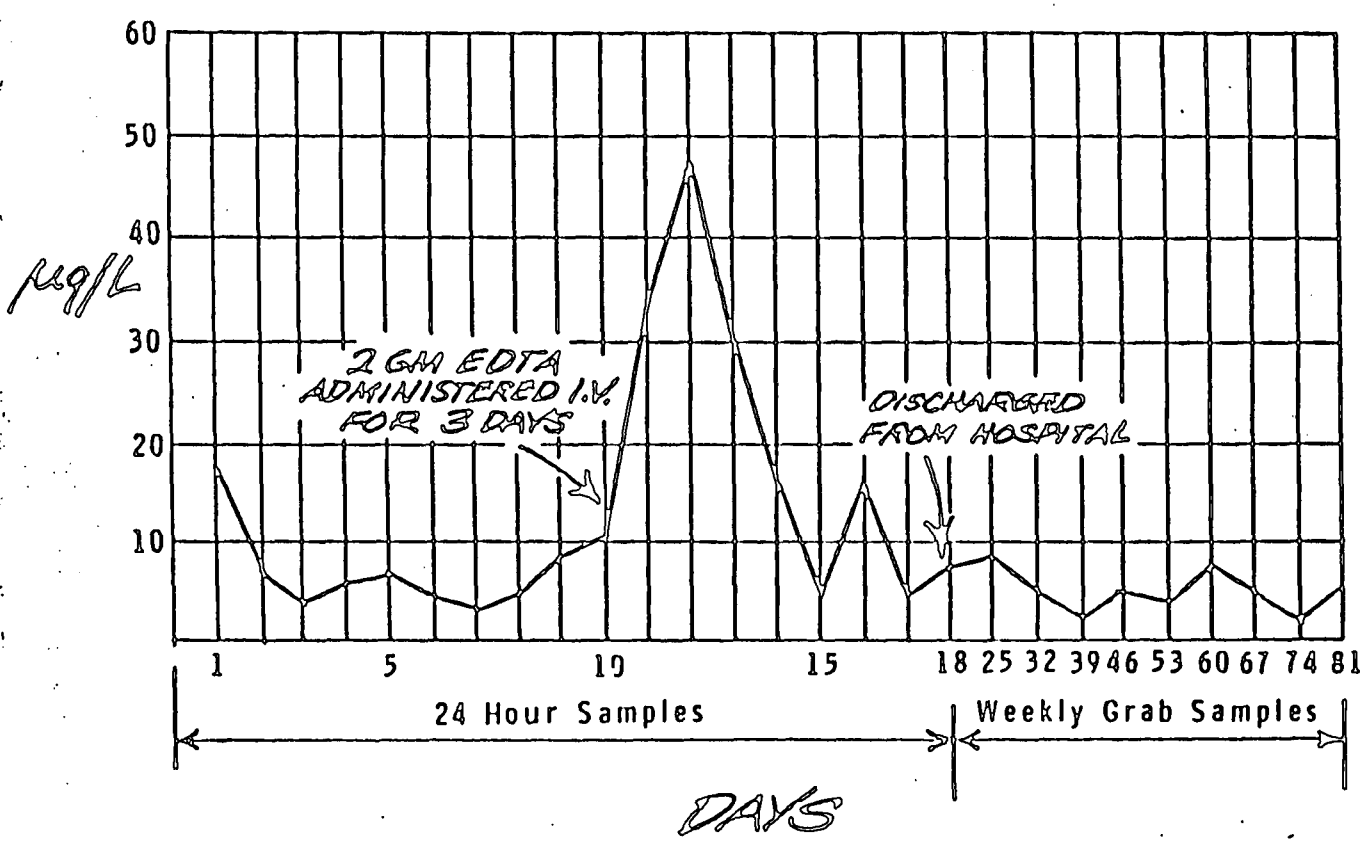
Each hospitalized employee was administered 2 gm of Calcium EDTA in 500 ml of dextrose intravenously on three successive days. Twenty-four hour urine collections were assayed for manganese. The average concentration of manganese in urine before, during, and after treatment is shown in Fig 6. The concentrations do not approach those reported in the Harrisburg cases. Nevertheless, the increased excretion certainly confirms manganese exposure and absorption and indicates mobilization following administration of the chelating agent.

Following discharge from the hospital and release for work in manganese-free areas, spot urine samples were collected weekly for ten weeks. Fig 6 also shows the manganese concentrations during this time. A second course of 2 gm of Calcium EDTA was given, on an ambulatory basis, to Cases 1, 2, and 4. There was little if any increased excretion of manganese. Subsequent weekly spot samples of urine have averaged below 6 µg/liter in all cases.

Three months after the time of the initial neurological examinations all five employees were re-examined. Cases 2 and 3 regained normal associated arm movements. No changes were noted in Cases 1, 4, and 5, and all continued to manifest the same degree of neurological deficit present on the initial examination. While their condition had not improved neither had it deteriorated. Improvement was noted in cases exposed to either manganese fume or ferromanganese dust but only when the neurological deficit did not exceed loss of associated arm movements.

In comparing the exposed and unexposed groups, no significant differences were noted in red blood cell counts, white blood cell and differential counts, hemoglobin levels, and hematocrits. There were seven instances of a history of pneumonia in the unexposed group as compared with eight in the exposed group. Employees having had pneumonia were not in the areas of highest exposure. Sick absence records also indicated no significant difference in the rate of sick absence for the two groups. In the exposed group there were no recorded absences for neurological

Fig 6. — Average urine manganese concentration in five patients—before and after EDTA.



problems except for Case 2.

Stippling of red blood cells has been reported as being a finding in manganism.[8] Blood smears of all employees were examined by a pathologist as a blind study. He reported two types of stippling: a coarse, granular type (reported as positive when one stipple cell was seen in ten high-power fields), and a fine, delicate stippling (reported as positive when seen as an occasional cell per slide). Table 4 reveals no significant difference in the number of persons in the two groups who demonstrated either type of stippling.

Table 5 shows manganese-in-urine concentrations by work area averaged 19 μg/liter in the Processing Plant, 6 μg/liter at the Blast Furnace Cast Floor, and 8 μg/liter at the Pig Casting Machine. The unexposed group averaged 7 μg/liter.

Table 5 further shows that the average manganese blood level of all exposed employees was the same as that of the exposed group, namely 3 μg/100 ml.

Table 3. — Manganese Dust-in-Air Concentrations by Position

Position	Number of Samples	Samples Exceeding Short Term Limit (STL)		Concentration (mg/cu m)		
		Number	% of Total	Low	High	Weighted-Average
Processing Plant						
Screen Plant Operator	51	29	57	0.98	34.7	6.3
Screen Plant Helper	53	37	70	0.88	61.5	12.9
Fork-Lift Operator	30	11	37	0.51	25.9	5.2
Payloader Operator	31	3	10	0.35	5.0	2.1
Craneman	52	9	17	0.18	47.7	4.4
Foreman	30	1	3	0.27	16.2	2.1

Table 4. — Summary of Stippling Observations

	Exposed Group	Unexposed Group
Coarse Stippling (1/10 HPF's)	6 out of 71	9 out of 71
Fine Stippling (Rare/Slide)	9 out of 71	2 out of 71
Total	15 out of 71	11 out of 71

Discussion

Several aspects of this study are worthy of comment. Those cases which responded favorably to EDTA treatment (2 and 3) regained normal associated arm movements, the loss of which constituted the only neurological deficit. It is suggested that this sign is a reversible rather than a permanent change, and could be of great importance from the standpoint of early detection and removal from exposure before the occurrence of irreversible central nervous system damage.

The lack of progression of the syndrome over six years lends support to the diagnosis of manganism, since parkinsonism of other etiology is a progressive disease.

The urine manganese concentrations averaged about three times higher in the dust-exposed group than in the unexposed group. While this appears to be a significant difference, it must be remembered that Cholak[9] reported urine concentrations as high as 600 μg/liter in persons with manganese exposure but without clinical evidence of manganism. Further, although the exposure of the Screen Plant Helper was twice that of the Operator, the urine concentration for the Helper was less than half that of the Operator. An attempt to correlate urine manganese concentrations with air con-

Table 5. — Manganese Blood and Urine Concentrations vs Air Concentrations by Position

Position	Weighted-Average Air Concentration (mg/cu m)		Blood Level (μg/100 gm)	Urine Level (μg/liter)
Blast Furnace				
Keeper	1.1		4	6
Blower	1.3		6	7
Hot Blastman	0.3		2	3
Turn Repair Pipework	1.3		2	10
Second Helper	0.5		2	8
First Helper	3.6		3	7
Cinderman	0.1		2	4
		Average	3	6
Pig Machine				
Tiller	4.4		2	6
Pourer	13.3		3	10
		Average	3	8
Processing Plant				
Screen Plant Operator	6.3		4	53
Screen Plant Helper	12.9		5	21
Fork-Lift Operator	5.2		3	8
Payloader Operator	2.1		5	9
Craneman	4.4		5	12
Foreman	2.1		2	4
		Average	4	19
Control Group		Average	3	7

centrations for each job position resulted in a correlation coefficient of 0.12. Thus there is very poor correlation between manganese exposure and manganese excretion in the urine. In Case 5, the Hot Blastman position, the manganese-in-air concentration was the second lowest exposure measured, yet the urine excretion of manganese (24-hour sample) was the only one to exceed normal prior to EDTA administration. Cholak[9] also states that the mean average for a group of unexposed individuals was 2 μg/liter with a range of 1 μg/liter to 7 μg/liter. The higher mean in our unexposed group (7 μg/liter) may be due to the fact that all steel workers in this plant may be exposed to slightly higher background levels than the normal population. Background atmospheric manganese concentration levels in the areas where the control group was located range from .001 to .025 mg/cu m. Finally, it must be recognized that fundamentally the bile is the primary metabolic pathway for excretion of manganese and the urine cannot very well be expected to reflect occupational exposure accurately. This is doubly apparent when we see manganism develop in the presence of normal urine manganese concentrations.

Equally lacking in correlation are blood manganese concentrations and exposure. The average manganese blood level of our exposed employees was the same as that of the unexposed group.

The development of manganism in one employee having a low exposure to manganese oxide fume (Case 5) suggests the possibility of hypersusceptibility of certain individuals inasmuch as others in similar positions and with equal or greater exposure did not develop manganism. This phenomenon is well known in toxicology. Unknown and unrecognized exposure away from the job site is another possibility. In any event, this case lends stress to the value of periodic physical examinations rather than examinations of biologic materials to detect early evidence of signs of manganism.

Conclusion

Although parkinsonism and manganism are indistinguishable, the detection of five cases among persons having an occupational manganese exposure, and in an age group in which parkinsonism is not expected, justifies the presumption of a causal relationship. The mobilization and excretion of large amounts of stored manganese after treatment with Calcium EDTA supports this presumption.

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*Threshold Limit Value. The maximum, average, atmospheric concentration of contaminant to which workers may be exposed for an eight-hour working day.

†Ceiling Value. A calculated value which may not be exceeded at any time; usually assigned to substances having a threshold limit value with little or no safety factor.

‡EDTA Calcium Ethylene Diamine Tetra-acetic Acid. A chelating agent chemically binding the manganese into a form excretable by the kidneys.